

PHOSPHORUS-31 IN VIVO HUMAN CARDIAC
MAGNETIC RESONANCE SPECTROSCOPY:
DEVELOPMENT OF MR SPECTROSCOPY TECHNIQUES

By

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A DISSERTATION PRESENTED TO THE GRADUATE SCHOOL
OF THE UNIVERSITY OF FLORIDA IN PARTIAL FULFILLMENT
OF THE REQUIREMENTS FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY

UNIVERSITY OF FLORIDA

1997

This dissertation is dedicated to
my mother, Soon Ran Kwon
my wife, Jung-Hee
and daughters, Dah-Song and Yeh-Song
and
Saeng Ji Lee, my mother-in-law
of blessed memory

ACKNOWLEDGMENTS

All work included in this dissertation would not have been possible without the guidance of Katherine Scott, Ph.D., my principal advisor. Dr. Scott is my scientific mentor and motivator. Her genuine enthusiasm for the pursuit of scientific knowledge and warm hearted patience were a real encouragement for me during the whole period of research.

I am obviously grateful to all the supervisory committee members for their excellent guidance, endurance and probing questions. Jeffrey Fitzsimmons, Ph.D., gave an overall picture of the whole body imaging system where this research has been done and advised me to follow the proper track of MR instrumentation. Richard Briggs, Ph.D., advised me to clarify the assumptions and the data obtained. His rigorous proofreading is also much appreciated. To J. Ray Ballinger, M.D., Ph.D., I am indebted not only for his advice and suggestions for all *in vivo* spectroscopic work and much help at the right moments, but also for his friendship and generosity. David Hintenlang, Ph.D., gave his thoughtful comments on my works. Christine Stopka, Ph.D., inspired me with her enthusiastic personality and shaped my dissertation by keen reviews.

I am grateful to all of my colleagues and friends who have contributed in so many ways toward the completion of this research. I am deeply indebted to Haejin Kang Ph.D., for introducing me to Dr. Scott and helping me since I first participated in the NMR realm. He furnished not only techniques necessary for MR spectroscopy but all the encouragement for life in Gainesville. Fellow

graduate student, Angela Bruner has given many days of her time to searching out the methods we looked for and shared thoughts and the excitement during many studies. I wish to recognize David Peterson who dealt with difficulties in the middle of engineering problems when I was trapped during building the second MR probe. He is an excellent RF coil engineer and well aware of Korean cultures. Carol Sweeney has shared with me lots of the excitement and frustration of MR spectroscopy. I wish to thank her for encouragement, for help in constructing phantoms and her thoughtful personality which was sufficiently insightful to help me out of some difficulties. Jim Scott advised me in the design of the second probe and gave me good insight. I am really grateful for his suggestions, and I was always delighted with his warm personality. Diana Garside, Ph.D., advised me in handling chemical substances. I wish to thank Chris Hunter and Teresa Lyles, M.S., for a secretarial support. Teresa Lyles' enthusiastic personality was an invigoration in Gator country. Jintong Mao, Ph.D. helped me to start to use EPIC® programming. To Soon Nyung Huh, Ph.D., who provided sound understanding the RF communication and to Marian Buszko, Ph.D., who discussed many aspects of MR techniques, I express my deep thanks.

I appreciate the comments offered by the following experts who furnished many helpful suggestions. Cecil Charles, Ph.D., gave an insight on how to implement the outer volume suppression with CSI. Ben Inglis, Ph.D., was willing to support me when I suggested a plan to apply the BIR-4 pulse to ^{31}P spectroscopy. Michael Garwood, Ph.D., kindly sent the BIR-4 pulse files. Napapon Sailasuta, Ph.D. and Qing Tan, M.S., provided source programs necessary for EPIC® pulse programming. Tom Raidy, Ph.D., shared his expertise in outer volume suppressions and short T_E spin echo. I am grateful for their kind and valuable help. I thank to Heung Kyu Lee, Ph.D., for

discussions on the MR imaging system. He always encouraged me throughout the research period.

I would like to recognize my former teachers and seniors. In particular, I am much obliged for the encouragement of Chang Soon Kang, Ph.D., my former graduate advisor in Korea, Chang Kun Lee, Ph.D., Jung Eui Kuh, Ph.D., and Hae Ryong Hwang, Ph.D., who always regard me with affection.

I also have to express my appreciation to all the volunteers who made a special effort to help my usually rushed requests. Thanks also go to Duk Won Kim, M.S., who spent a lot of time in helping me organize the manuscript files.

I am most grateful to my family in my country who so generously encouraged me to study abroad even in adversity. I am very much indebted to my mother, Soon Ran Kwon. Surely, her prayer was responded. I owe a tremendous debt of gratitude to my sisters, Hwa Seung and Hae Ja, for encouragement and patience and for a good deal of moral support throughout my study. My special thanks go to Mr. Dong Du Shin for rendering support and giving many days of his precious time to me.

I wish to recognize my father-in-law, Chun Duk Oh, for all he has given so unselfishly in the most heartbreaking days in his life, as have my sister-in-law Jee Hee Oh and Young Hoon Kim for encouragement when it was most needed.

No doubt my greatest debts are to my family. My daughters Dah-Song and Yeh-Song have turned our lives into truly happy Songs. Without my wife, Jung-Hee, nothing would have been possible. Her love made all my days a happy experience. I give her my loving appreciation.

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SYMBOLS AND ABBREVIATIONS

2,3-DPG	2,3-diphosphoglycerate
γ	gyromagnetic ratio
AIT	Available imaging time
AP	Array processor
ATP	Adenosine triphosphate
BAM	Bulk access memory
CPU	Central processing unit
CSI	Chemical shift imaging
CV	Control variable
DAB	Data acquisition board
DRESS	Depth Resolved Surface coil Spectroscopy
ECG	electrocardiogram
FLAX-ISIS	Fourier Series Window Longitudinally modulated and using adiabatic excitation with ISIS
GPC	glycerophosphoryl choline
GPE	glycerophosphoryl ethanolamine
HEP	High energy phosphate
IPG	Integrated pulse generator
ISIS	Image Selective <i>In vivo</i> Spectroscopy
MDPA	Methylene diphosphonic acid

MRS	Magnetic resonance spectroscopy
NEX	Number of excitations
OVS	Outer volume suppression
PCr	Phosphocreatine
PDE	Phosphodiester
Pi	Inorganic phosphate
PME	Phosphomonoester
PRESS	Point Resolved Spectroscopy
RF	Radio frequency
ROI	Region of interest
SLR	Shinnar-Le Roux algorithm
SAR	Specific absorption rate
SNR	Signal-to-noise ratio
SPARS	Spatially Resolved Spectroscopy
STEAM	Stimulated Echo Acquisition Mode
T_1	Spin-lattice relaxation time
T_2	Spin-spin relaxation time
T_E	Echo time
TG	Transmitter gain
TPS	Transceiver processing and storage
T_R	Repetition time
T/R	Transmit-receive
VOI	Volume of interest
VSE	Volume Selective Excitation

Abstract of Dissertation Presented to the Graduate School
of the University of Florida in Partial Fulfillment of the
Requirements for the Degree of Doctor of Philosophy

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MAGNETIC RESONANCE SPECTROSCOPY:
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August, 1997

Chairman: Katherine N. Scott

Major Department: Nuclear and Radiological Engineering

This study was undertaken to develop techniques for ^{31}P *in vivo* human cardiac magnetic resonance spectroscopy (MRS) in a 1.5 tesla whole body MR imager. MR spectroscopy can be used for the noninvasive evaluation of the metabolic status of cardiac or skeletal muscle. In order to solve problems specific to ^{31}P MR spectroscopy of the intact human heart, the following tasks had to be accomplished: to build MR probes with high sensitivity, to develop an appropriate localization technique, to reduce the artifacts produced by the heart contractile motion, and to provide relevant quantification of the spectral data.

The surface coil was chosen as the MR probe for its inherent high sensitivity. Two surface coils, COIL A and COIL B, of appropriate diameter were built to maximize the signal detection from the adult human heart at a representative distance below the chest wall. COIL A was built as a transceiver

and was doubly tuned to proton and ^{31}P MR frequencies to carry out both B_0 field shimming and ^{31}P spectroscopy. COIL B was built as a receiver and transmitter coil assembly. The large transmitter of COIL B was coaxially placed to produce a homogeneous B_1 field over the sensitive volume of the receiver coil, and the mutual inductance between transmitter coil and receiver coil was minimized by diode-blocking circuits.

Two major localization techniques were developed. First, 2D outer volume suppression (OVS) using a cos-sinc presaturation pulse was combined with 1D image selective *in vivo* spectroscopy (ISIS). Second, the Fourier spectroscopic imaging method was applied to deep-seated regions of interest, from the intercostal muscle to the myocardium. The spatial localization of ^{31}P spectra was improved by combining chemical shift imaging (CSI) with OVS using a Shinnar-Le Roux saturation pulse.

The pulse sequences were tested both on home built phantoms and human subjects. The artifacts arising from cardiac contractile motion were minimized using ECG cardiac gating which synchronizes pulses to the patient's heart beat.

The effects of partial saturation and blood contamination were evaluated to obtain precise phosphocreatine (PCr) to adenosine triphosphate (ATP) ratios from *in vivo* human cardiac ^{31}P spectra.

After accomplishing the aforementioned tasks, a protocol was developed for human ^{31}P MR cardiac spectroscopy.

CHAPTER 1 INTRODUCTION

Existing Knowledge in This Area

Phosphorus-31 magnetic resonance spectroscopy (MRS) can be used to investigate the metabolism and bioenergetics of tissue and organs non-invasively. The levels of high energy phosphates (HEPs) are important indicators which can reflect pathological changes occurring in tissues such as skeletal muscle and heart muscle. ^{31}P MR spectroscopy also provides the means to determine the turnover of HEPs, which correlates more dynamically with organ function than the steady-state tissue HEP levels^{1,2,3}. Thus, the status of cardiac disorders can be evaluated by ^{31}P MR spectroscopy⁴.

Since the early studies of human cardiac spectroscopy in infants⁵ and in adults⁶, noninvasive ^{31}P cardiac spectroscopy has been used to detect several phosphorus containing metabolites including adenosine triphosphate (ATP), phosphocreatine (PCr), phosphomonoester (PME) and inorganic phosphate (Pi). The following studies have been performed: (1) HEP changes during the cardiac cycle along with phasic change in cardiac work and perfusion⁷, (2) evaluation of metabolic response of the heart to large changes in workload^{2,8,9}, (3) metabolic change associated with myocardial ischemia and infarction^{10,11,12}, (4) a study of cardiomyopathic processes that may involve changes in the availability or utilization HEP^{13,14}, and (5) early and sensitive indication of rejection after cardiac transplantation¹⁵.

The difficulties of spatial localization have limited the number of cardiac ^{31}P NMR studies in humans. However, several investigators have shown the feasibility and potential of this technique in selected circumstances.

Normal myocardium: The study of myocardial energetics has been pursued with isolated perfused heart and *in vivo* animal preparations with both surface coils and catheter coils. The first human cardiac spectra were obtained by Bottomley using depth resolved surface coil spectroscopy (DRESS)¹⁶, followed by several studies using the rotating-frame technique⁶, image selective *in vivo* spectroscopy (ISIS) and/or Fourier spectroscopic imaging^{17,18,19}. Most studies obtained PCr/ATP values under normal and under stressed conditions^{20,21}. Several applications of localization techniques have been used such as *Fourier Series Window Longitudinally modulated* and using *adiabatic excitation* with ISIS (FLAX-ISIS)²², spectroscopic imaging for observation of cardiac lipid²³, and 3-D spectroscopic imaging²⁴.

Myocardial ischemia: The Fourier series window experiment was used to examine changes in the subendocardium and subepicardium during ischemia in animal studies^{12,25,26}. Employing DRESS to examine patients following myocardial infarction, Bottomley and associates found abnormal PCr/Pi ratios with some evidence that the abnormal metabolism was primarily localized in the subendocardium of some patients²⁷.

Dilated cardiomyopathies: Using only a surface coil for localization in an 8-month-old female child with massive cardiomegaly, Whitman and associates found the PCr/Pi ratio to be 1.0, a value half that of a normal control²⁸. Furthermore, glucose or carbohydrate loading raised this ratio to 1.8, suggesting that MRS could guide therapy in selected cardiac disorders.

Hypertrophic cardiomyopathy: In studies of hemodynamically compensated patients, using the rotating-frame technique, Rajagopalan and associates²⁹ and Schaefer and associates¹⁸ did not find any abnormalities in the PCr/ATP ratio. However, two patients in each group did have abnormally large resonances in the phosphodiester (PDE) region corresponding to abnormalities in the membrane constituents glycerophosphoryl choline (GPC) and glycerophosphoryl ethanolamine (GPE). These preliminary data suggest that membrane abnormalities due to the myopathic process may be detectable by ³¹P MRS.

Cardiac transplantation: Animal studies have demonstrated alterations in the HEP metabolism of rejecting hearts that temporally correspond to the degree of rejection^{15,30}. Using 1-D spectroscopic imaging, Herfkens and associates³¹ studied several patients following cardiac transplantation. When compared with biopsy results, there was an association between increasing Pi and decreasing PCr with the degree of rejection.

In summary, numerous attempts to implement ³¹P *in vivo* cardiac spectroscopy have been carried out. However, to date, there is no universally accepted technique. Techniques vary with the MR system used, the subjects studied and the parameters to be measured. The techniques employed leave much to be desired, in terms of signal-to-noise ratio, spectral resolution and spatial resolution.

Statement of the Problem

The intact human heart is one of the most difficult organs from which to acquire an MR spectrum. (1) The heart is irregularly shaped and some parts are

located deep within the mediastinum. Thus it is necessary to use spatial localization techniques, which tend to reduce the signal-to-noise ratio (SNR). (2) The heart is in constant motion, both from its own contractions and from respiration. The artifacts and signal degradation resulting from the cardiac motion can be suppressed by cardiac gating. However, this prolongs the examination time. (3) Although a heart is a large organ, the cardiac muscle occupies only a fraction of the volume of the heart. In addition, some cardiac structures of clinical interest are small and give weak signals. (4) The phosphorus spectrum of heart muscle is very similar to the overlying intercostal muscle. The blood in the chambers of the heart gives a strong 2,3-diphospho-glycerate (2,3-DPG) signal that obscures the Pi resonance of the cardiac muscle, and the blood also contributes to the ATP signal. (5) The levels of HEP are very well regulated in the heart. Therefore, changes in HEP arising from pathological conditions and/or from drug effects are much smaller in the heart than in skeletal muscle.

This study is designed to furnish methods to carry out the ^{31}P cardiac MR spectroscopy in a 1.5 tesla whole body imager by developing techniques beyond those that have been provided to date.

Specific Aims of the Proposed Research

In many abnormalities in heart energetics including dilated cardiomyopathy, left ventricular hypertrophy, valvular disease, heart transplants, myocardial infarction, or reversible ischemia, deviation in the PCr/ATP ratio or metabolic concentration from normal healthy control has been observed. This study specifically aims to develop techniques to evaluate

relative PCr/ATP ratio in human *in vivo* MR cardiac spectroscopy in a 1.5 tesla MR whole body imager.

Feasibility of Surface Coil Spectroscopy

The inherent high sensitivity of the surface coil will provide the best probe type for ^{31}P MR cardiac spectroscopy. *In vivo* phosphorus metabolites give only a factor of 10^{-5} signal-to-noise ratio of tissue water signal. In this study, surface coils will be used for acquiring the ^{31}P MR signal and also the proton signal for B_0 field homogenization.

Cardiac Gating MR Experiment

The ECG cardiac gating will minimize the motion artifacts arising from the contractile motion of the heart. The motion artifact will be most severe for specific spectroscopic localization techniques, such as Image Selective *In vivo* Spectroscopy (ISIS), which will be one of the pulse sequences used in this study. Without cardiac gating, it will be very difficult to obtain scout MR images, to obtain a consistent tissue water signal for B_0 field shimming, and to obtain a localized ^{31}P MR signal.

Outer Volume Suppression and its Hybrid

A saturation pulse in conjunction with the surface coil will suppress the MR signal from the volume outside the region-of-interest. The same saturation pulse can be combined with other single voxel localization techniques to improve signal-to-noise ratio and to reduce the motion artifacts.

Several saturation pulses will be considered. After a proper pulse is chosen, parameters will be optimized. The performance of the saturation pulses

and their hybrid pulse sequences will be examined and verified by both phantom and in vivo studies.

Chemical Shift Imaging with Outer Volume Suppression

One or two dimensional chemical shift imaging technique will be applied to obtain a spectral map in the given anatomical slices. To improve the spatial selectivity, a presaturation pulse will be applied before the excitation pulse. The presaturation pulse will be selected for the best localization for each orientation.

Quantitation

The PCr/ATP ratio will be evaluated based on the assumption that the area of a spectral peak is directly proportional to its chemical concentration³². Because the repetition time, TR, is not long enough to reach complete relaxation, the PCr/ATP will be corrected for the partial saturation effect using either reported T_1 or direct measurement of partial saturation for each subject.

CHAPTER 2 SURFACE COIL SPECTROSCOPY

Review of the Literature

For *in vivo* NMR spectroscopy, the signal-to-noise ratio with appropriate spectral resolution and the localization achieved are the two major concerns. These problems are especially important for *in vivo* detection of biologically significant nuclides which occur in low concentrations. Since 1980 when the surface coil was introduced, the surface coil has found wide-spread application in *in vivo* spectroscopy as a result of its inherently high degree of localization and high sensitivity over regions close to the coil³³.

In vivo ³¹P MR spectra from intact human hearts have been detected with surface coils because of superior sensitivity relative to whole-body coils³⁴. A tuned circular surface coil can produce at least 90% of the maximum signal-to-noise ratio achievable by any optimized coil geometry for detecting a signal source at a given depth in the body³⁵. A surface coil of diameter approximately equal to the depth of the signal sources of interest produces the optimum signal-to-noise ratio, assuming that the sample is the dominant noise source³⁶.

The receiver coil is mainly a circular solenoid^{37,38,39,40,41,42,43,44,45} or less frequently another type of coil^{46,47} either single tuned ^{37,38,42,47}, or doubly tuned to both ¹H and ³¹P frequency ^{39,40,45,46}. A surface coil can be used in the single-coil-mode, i.e. used for both transmission and reception ^{37,39,40,45}, or in the reception mode as a separate receiver ^{38,41,42,47}.

Design and Building of Surface Coils

The principle of reciprocity⁴⁸ describes the oscillating signal voltage $S(t, r)$ induced in an NMR receiver coil by a precessing magnetic moment $\mathbf{M}$ at r :

$$S(r, t) = -\frac{\partial}{\partial t}(B_1(r) \cdot M(r, t))$$

where $S(r, t)$ is signal voltage, B_1 is the magnetic field produced by unit current, and $\mathbf{M}$ is a precessing magnetic moment.

When a sample is excited on or near resonance by the application of a transverse RF magnetic field B_1 , the magnetization produced in the XY plane, M_{xy} , is related to $(B_1)_{xy}$ through the flip angle α :

$$M_{xy} = M_z \sin \alpha,$$

$$\alpha = \gamma t_p I(B_1)_{xy}$$

where M_z is the amplitude of the longitudinal magnetization just prior to excitation, γ is the gyromagnetic ratio, t_p is the transmitter pulsewidth, and I is the current through the coil. When a surface coil is used as the transmitter, the highly inhomogeneous $(B_1)_{xy}$ of the surface coil results in a wide distribution of flip angles within the sample:

$$\alpha(r) = \gamma t_p I(B_1)(r).$$

This distribution of spin flip angles produces a dependence of the transverse magnetization amplitude on the spatial coordinate.

$$M_{xy}(r) \propto \sin \alpha(r).$$

Although surface coil excitation does not produce a single flip angle over the entire sample, the spins in given restricted regions of the sample; corresponding to regions of iso- B_1 , can be given specific flip angles through the appropriate selection of t_p or $I(B_1)$. The spins at the location 0.77 radii deep along the axis of the coil experience half the field strength that is experienced at the coil center⁴⁹.

COIL A: Transmitter/Receiver Surface Coil

For the cardiac spectroscopy study, the first surface coil (COIL A) was used as a transceiver despite the rapid decrease of the signal intensity profiles with distance due to the dual dependency of transmitter and receiver. The reasons are the following: First, it is simple to build, and can easily be mounted at the precise position on the chest measured by the scout MR image. Second, although B_1 is highly inhomogeneous in both magnitude and direction, when the surface coil is used in the single-coil mode on or near resonance, the phase angle between the excitation field and the reception field is the same at every point r ^{33,50,51}. Since the phase of M_{xy} is determined by the phase of the excitation field B_1 , the phase angle between the receiver B_1 and M_{xy} will be constant at every point over the sample volume⁵¹, and MR signals from all

parts of the sample will be in phase and will add coherently over the excitation volume of the surface coil.

When the same coil is used for both transmission and reception (single-coil mode), the signal amplitude distribution achieved as a result of surface coil excitation and reception with a homogeneous sample is described by⁴⁹

$$S(r) \propto B_1(r) \sin \alpha(r),$$

$$\alpha(r) = \alpha_0 \frac{(B_{1xy})(r)}{(B_{1xy})_0},$$

where $\alpha(r)$ is expressed relative to the flip angle experienced at the center of the coil, α_0 , and B_{10} represents the field at the center of the coil. The receiver $B_1(r)$ is equivalent to the transmitter $B_1(r)$, and the effect of the dual dependency of the signal amplitude on $B_1(r)$ results in the more rapid decrease of the signal-intensity profile with distance compared to that of the B_1 profiles.

Doubly Tuned Circuit

It was found that the shimming of the B_0 field is extremely difficult due to the high noise level when the body coil is employed to detect the water signal in the localized region of the left ventricle. In order to enhance the MR signal from the heart, the surface coil was used to receive the signal, because of its enhanced localized sensitivity relative to the body coil. This raises the need of a coil which is doubly tuned to both proton and ^{31}P resonance frequencies. When the B_0 field is homogenized by AUTOSHIM, which uses gradient-recalled echo pulse for rapid shimming, the body coil is generally

used. However, the doubly tuned surface coil also can be used to generate a B_0 field map and to fit the linear shim gradient coefficients.

Figure 2.1 represents the circuit diagram of COIL A. The design is based on a standard capacitively coupled resonant tank circuit with the trap circuit added as Schnall proposed for double tuning⁵². By using an additional pair of inductive and capacitive components (L and C_4), the proton frequency (63.9 MHz) is created. The Schnall circuit was chosen because the high frequency can be optimized without losing optimum low frequency sensitivity and because weak coupling between the two frequencies makes the coil easy to build.

COIL B: Separate Transmitter and Receiver Coil

The transmitter and receiver coil or tranceiver coil, as COIL A, produces an inhomogeneous B_1 excitation profile. The resultant wide distribution of flip angles limits application for specific localization for *in vivo* cardiac spectroscopy. When the presaturation pulse is applied for the outer volume suppression (OVS), the flip angle over the volume to be suppressed surrounding the ROI is expected to be the same. This condition is hard to achieve with a small excitation surface coil. Moreover, it is almost impossible to produce homogeneous excitation when the surface coil plane is not parallel to the magnet frame coordinate, because the magnet frame coordinates determine the X, Y and Z gradients, and B_1 iso-contours of the surface coil will not be parallel to any of these coordinate axes.

Another experiment which is compromised by an inhomogeneous flip angle is chemical shift imaging. Since all localized volumes at all depths are

simultaneously excited when phase encoding is done along the coil axis, the transmitter power can not be adjusted to the depth of the subject which experiences different flip angles depending on the spatial position.

One solution to this problem is homogeneous excitation while maintaining the high signal sensitivity with the surface coil receiver. A saddle type coil can be used as a homogeneous B_1 transmitter, with a surface coil receiver positioned orthogonally to minimize magnetic coupling between the two coils. A large saddle coil that would fit over the chest would require more power than the system can deliver. Instead, a coaxial coplanar surface coil of larger diameter can be used as a separate transmitter, and a smaller diameter coil used as a receiver. The signal-amplitude distribution of homogeneous excitation and surface coil reception is described by⁴⁹

$$S(r) \propto B_1(r) \sin \alpha(r),$$

$$\alpha(r) = \alpha_0 \frac{B_{1x}(r)}{B_{1x0}},$$

where the x axis represents depth into the sample, and the function of the receiver $(B_1)_{xy}(r)$ becomes a function of $(B_1)_x(r)$.

The uniform B_1 field in turn results in transmitter/receiver phase mismatch when a small receiver coil is used. This in turn cancels out the signal in part of the sample. For the case of a coaxial and coplanar surface coil, the signal cancellation is less severe than for the homogeneous excitation experiment^{53,54}.

If the flip angle over the sample is assumed uniform, the penetration depth relative to the transceive coil will increase, because total signal from the homogeneous excitation experiment is obtained from a deeper sample volume than from the single coil experiment. In equilibrium, however, the total signal intensities are comparable in both experiments⁵⁵.

Coil Building

Because the best sensitivity is achieved when the coil diameter roughly matches the depth of the tissue of interest⁵⁶, a circular reception surface coil of diameter 5 to 10 cm is optimum for reaching the anterior myocardium 5 to 10 cm into the chest ³⁵.

COIL A

The circuit consists of a 2-turn, 7.5 cm diameter solenoid coil of 16 AWG copper wire (1.4 mm in diameter), which is doubly tuned to 25.8 MHz for ³¹P and to 63.9 MHz for proton frequency at 1.5 tesla. Johanson variable air gap capacitors were used, and the coil was matched to 50 Ω (C₁ and C₂). When the coil was matched, the unloaded/loaded Q ratios were 0.7 and 0.6 for ¹H and ³¹P, respectively.

The decrease in the RF field strength with depth is illustrated in Figure 2.2 which is estimated along the axis perpendicular to the plane of and through the center of the surface coil by⁵⁷

$$(r^2 + d^2)^{-3/2}$$

where r is the coil radius and d is the depth from the coil surface. Figure 2.3 shows COIL A tuned to proton and ^{31}P MR frequency.

COIL B

The coil set consists of two coaxial and coplanar coils: a one turn small solenoid - 7.5 cm in diameter and a one turn large solenoid - 25 cm in diameter. Both coils were made of 8 mm wide 3M™ copper strip. The coils were tuned to 25.87 MHz, the ^{31}P MR frequency at 1.5 tesla. For the transmitter coil, the capacitors were distributed at equal intervals (34 cm) around the solenoid in order to minimize dielectric interactions and losses between the patient and coil relative to the lumped-element design⁵⁷. The unloaded/loaded Q ratios were 0.6. Figure 2.4 shows the circuit diagram of COIL B.

To eliminate coil coupling by mutual inductance, the solenoid of the transmitter was cut, and a crossed diode pair of UM9415™ was inserted to turn off the transmitter during ^{31}P reception (B_2 in Figure 2.4). The receiver coil contains a block loop with diode MBD301™ and a choke across distributed capacitors in a small resonant loop tuned to the ^{31}P frequency to turn the receiver off during transmission (B_1 and C_4). The separation was -24 dB for inductive coupling for receiver during transmission. The separation of transmitter from the receiver during reception was -21 dB. The COIL B was built as shown in Figure 2.5.

In Figure 2.6, COIL A (center) and COIL B (right) are shown. In addition to COIL A and COIL B, another doubly tuned transceiver coil which is 15 cm in diameter is also shown. This coil was built prior to the design of COIL A and COIL B. The transmitter power was not enough to drive the 15 cm solenoid coil. The characteristics of COIL A and COIL B are summarized in Table 2.1.

Table 2.1 Comparison of COIL A and COIL B

	COIL A		COIL B	
Type	Transceiver 2 turn solenoid doubly tuned ($^1\text{H}/^{31}\text{P}$)		Transmitter-Receiver 1 turn solenoid Tx 1 turn solenoid Rx single tuned (^{31}P)	
Q	Loaded	38 (^{31}P)	Loaded	35 (^{31}P)
	Unloaded	64 (^{31}P)	Unloaded	55 (^{31}P)
	Loaded	30 (^1H)		
	Unloaded	41 (^1H)		
Separation	-	-	Tx to Rx	-24 dB
			Rx to Tx	-21 dB

In summary, a $^1\text{H}/^{31}\text{P}$ doubly tuned surface coil was selected as the first MR radiofrequency probe, COIL A. Schnall's doubly-tuned circuit was chosen because of its performance characteristics. The same surface coil is used for both transmission and reception. Coil A is preferred due to its simplicity and its in-phase characteristics, even though some loss of signal intensity occurs.

The second coil, COIL B, was built for the purpose of delivering a uniform excitation B_1 field. A small coil with the size optimized for signal reception was used as a receiver coil. A larger coaxial coplanar coil was also built to produce a more uniform flip angle distribution. Each of the loops has a diode block to remove mutual interaction during transmission and reception.

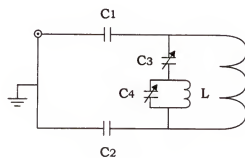
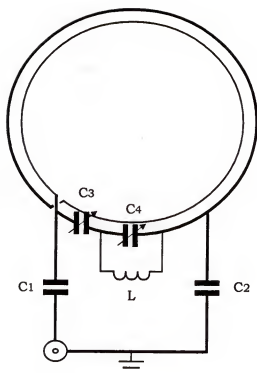


Figure 2.1 Circuit diagram of COIL A.

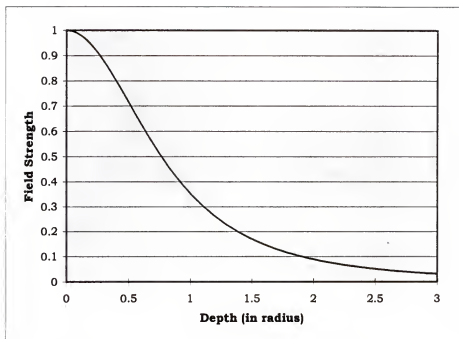


Figure 2.2 Field strength vs. distance from the coil.

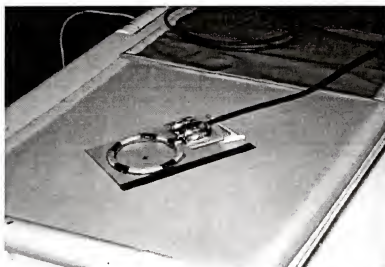


Figure 2.3 COIL A : Doubly tuned transceiver coil.

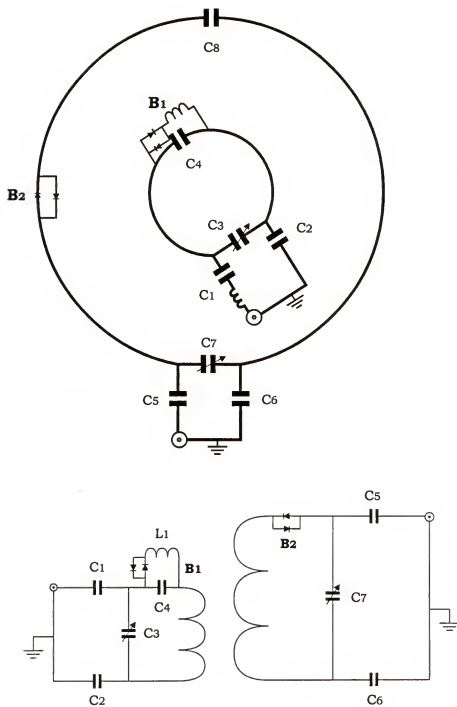


Figure 2.4 Circuit diagram of COIL B.



Figure 2.5 COIL B : Separate-transmitter/receiver coil.

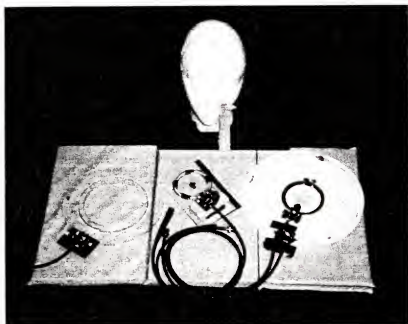


Figure 2.6 COIL A (center), COIL B (right) and large transceiver coil.

CHAPTER 3 LOCALIZATION TECHNIQUES FOR CARDIAC SPECTROSCOPY

Review of Localization Techniques for Cardiac Spectroscopy

Among the many schemes to provide anatomic localization, the following four have been successfully applied to studies of the human heart. They all use a surface coil on the chest for signal transmission and reception and provide localization by spatially encoding nuclei using either the varying radio frequency B_1 field produced by a surface coil or the varying static B_0 field by gradient coils in the magnet.

Rotating Frame

The rotating frame technique utilizes the changes in the RF B_1 field produced by the surface coil. With increasing distance from the coil along its axis, the B_1 field produced by the coil decreases in intensity at a known rate. If the coil excitation pulses are lengthened for each successive data acquisition, a series of spectra are acquired that correspond to varying distances from the coil. Although this technique is simple in that no gradients from the magnet are required for localization, it lacks the flexibility to choose appropriate volumes.

This technique has been applied with success to investigating metabolic heterogeneity across the myocardium in open chested animal experiments. When the rotating frame probe was attached directly to the ventricular wall, the

localization was with respect to the probe, and hence the outer surface of the heart muscle^{58,59,60,61}.

Depth Resolved Surface Coil Spectroscopy (DRESS)

The DRESS technique uses both B_1 and B_0 for localization. The nuclei in a plane parallel to the surface coil are selected by a B_0 gradient excitation sequence and detected by the surface coil. The depth of the region of interest is defined by the selective excitation, whereas its lateral dimensions are determined by the sensitive volume of the surface coil⁶². This technique has the advantage of selecting a plane from the MR image prior to spectroscopy, but it cannot localize the volume of interest in the lateral dimensions parallel to the coil. Thus there is a potential for significant signal contamination from undesired tissues and potential loss of sensitivity from the gradient refocusing pulse required before acquisition of the signal.

Image Selective *In Vivo* Spectroscopy (ISIS)

ISIS is a B_0 technique that allows selection of a 3-D volume of interest. This volume is typically chosen from a magnetic resonance image of the subject obtained immediately before the spectroscopy examination. A series of magnetic field gradients and RF pulses are used to select the volume of interest (VOI) in space, which is relatively independent of the position or the sensitivity profile of the surface coil^{63,64}. ISIS localizes signals to a small volume in the sample by a procedure of successive subtraction of the large signals from the entire sample in a sequence comprised of at least 8 repetition time (T_R) intervals. Its spatial precision allows the calculation of absolute metabolite concentrations from the VOI⁶⁵. This technique also has the advantage in its

flexibility to choose a volume. However, the requirement for adding signals from multiple acquisitions makes it more sensitive to degradation of the signal due to either cardiac or respiratory motion.

Spectroscopic Imaging

Spectroscopic imaging employs phase-encoding gradients in 3-D to define an array of voxels⁶⁶. In contrast to ISIS, spectroscopic imaging allows the selection of voxel positions from a corresponding image after data acquisition. Thus, spectra can be reconstructed from multiple VOI chosen to correspond to selected anatomic regions. Spectra can be summed from multiple volumes or displayed as a metabolic map.

This technique has the advantage of providing relative insensitivity to motion, since it does not depend on cancellation of signal to provide localization. Moreover, the spectroscopic imaging technique does not have an error from chemical shift offset which introduces a misregistration of the particular chemical shift resonance in the slice selected by the frequency selective pulse in the presence of the pulsed gradient. However, its spatial selectivity is not as good as that of ISIS. Therefore this technique results in more contamination from tissues outside the chosen volume.

The Techniques Developed for This Study

Outer Volume Suppression Pulse

The *Image Selected In vivo* Spectroscopy (ISIS) technique⁶³ yields sharp spatial delineation and insensitivity to T_2 -distortion. This is a major advantage for *in vivo* ^{31}P MR spectroscopy where T_2 times of metabolites are short.

However, when the ISIS technique is used for the heart or abdominal organs, the usefulness of this technique is limited due to the cancellation error from incoherent motion of the subject during the 8 scan period.

Outer volume presaturation of magnetization (OVS) can be an alternative localization for *in vivo* ^{31}P MRS, because this method is not T_2 weighted. The degree of suppression of the signal from the outer volume depends largely upon the accuracy of the tip angle of the RF presaturation pulses. Because of the large B_1 field gradient of the surface coil, OVS is difficult to use in conjunction with a surface coil. Several methods for reducing the inaccuracies in localization of OVS have been carried out at the expense of a longer localization time⁶⁷.

For example, the use of the BIR-4 adiabatic pulse was proposed to accomplish the volume suppression. The integrated OVS-ISIS sequence using BIR-4 plane rotation adiabatic pulse^{68,69} decomposes the longitudinal magnetization outside of region-of-interest. In this study, the use of the BIR-4 pulse was examined. The phase modulated plane rotation BIR-4 pulse⁶⁸ is shown in the time domain in Figure 3.1(a). The same pulse was simulated based on the Bloch equation in the frequency domain and is shown in Figure 3.1(b). It is clear from Figure 3.1(b) that the longitudinal magnetization, M_z , outside a certain bandwidth is modulated like noise which can be completely eliminated by the phase cycling.

The most significant problem in using the BIR-4 pulse is that the BIR-4 demands very high level of B_1 field to meet the adiabatic criterion. According to the Bloch simulation, the BIR4 pulse of 3.2 ms requires a maximum B_1 amplitude of 1.44 gauss in the middle of the pulse to achieve reasonable slice selection. It is four times higher than that of the standard GE ISIS adiabatic

inversion pulse. Another problem is that this sequence requires 64 step phase cycling to accomplish complete outer volume suppression.

In order to take advantage of the useful features of ISIS and OVS for cardiac ^{31}P spectroscopy, a hybrid combining ISIS and OVS was developed, in which one dimensional ISIS is coupled with outer volume presaturation in the other dimensions.

OVS Pulse

Outer volume suppression utilizes RF saturation to destroy the net magnetization in the volume outside the region of interest (ROI). The saturated region is then no longer able to produce a signal until the longitudinal magnetization recovers. The saturation is achieved by $\pi/2$ excitation pulses followed by a large dephasing gradient. This suppresses the signal produced by the magnetization in a slice.

The important magnetization component for saturation pulses is M_z . After the saturation pulse and dephasing gradient, all transverse magnetization is assumed to be dephased. The saturated magnetization should be left with no M_z so that subsequent excitation pulses will produce no signal. The unsaturated magnetization should be left with its full M_z , so that when subsequently excited it will produce its full signal.

OVS pulse design (I): Cos-sinc pulse

In order to isolate the ROI by suppressing the outer volume signal, the saturation RF pulse shape has to be tailored in such a way that it excites only the outer region. One such profile consists of two slices to be excited simultaneously leaving the ROI located between these two slices unperturbed.

For a small tip angle, the shape of the saturation RF pulse can be determined by taking the inverse Fourier transform, analytically or numerically, of the desired response profile in one dimension.

The analytical RF field, $B_1(t)$, corresponding to the ideal response of such a profile, can be obtained by the Fourier transform relation

$$B_1(t) = \int_{-(\nu_1+\nu_2)}^{(\nu_1+\nu_2)} M(\Delta\nu) \exp(i 2\pi\Delta\nu t) d(\Delta\nu),$$

where M is the magnitude of the transverse magnetization and $\Delta\nu$ is the frequency offset of the B_1 field. After performing the integration for the desired $M(\Delta\nu)$, the RF field can be expressed as an even function⁷⁰

$$B_1(t) = C \operatorname{sinc}(2\pi\nu_2 t) \cos(2\pi\nu_1 t),$$

where C scales the tip angle. The shape of the RF field given by the equation above is a frequency modulated sinc function. The modulation frequency ν_1 of $\cos(2\pi\nu_1 t)$ determines the width of the ROI. The frequency ν_2 , the width of the central lobe of the sinc function, determines the diameter of the outer region to be excited and saturated. An alternative wave form is obtained on Fourier transformation of the odd function, yielding a sin-sinc pulse, the amplitude of which varies as⁷¹

$$B_1(t) = -i D \operatorname{sinc}(2\pi\nu_2 t) \sin(2\pi\nu_1 t)$$

These pulses can be compromised by T_1 effects⁷² and by samples which are large relative to the receiver coil for which the excitation band of the pulse may not be wide enough to eliminate signals from the edge of the sample⁷⁰.

Pulse generation: A program was written to generate the cos-sinc pulse using Matlab® software. The pulse resolution and modulation frequencies of both cosine and sinc function are entered, and then the program generates a pulse in a binary form as well as a text file. The source code and the text file generated are attached in the Appendix. Figure 3.2 shows the output of the program illustrating the saturation pulse and its Fourier transformation. If this pulse is applied twice, the M_z magnetization is saturated more completely in the excitation band. Figure 3.3 shows the response of the Bloch simulation which is based upon the Shinnar-Le Roux (SLR) transformation⁷³. The response signal was obtained from the elements of the rotation matrices,

$$M_{xy}^+ = 2 \alpha^* \beta M_0,$$

where α and β are the Cayley-Klein parameters

$$\alpha = \cos \phi/2 - i n_z \sin \phi/2$$

$$\beta = -i (n_x + i n_y) \sin \phi/2.$$

These parameters are elements of the 2×2 unitary matrix which represents the solution of the Bloch equation when neglecting relaxation⁷⁴ such that

$$Q = \begin{bmatrix} \alpha & -\beta^* \\ \beta & \alpha^* \end{bmatrix}$$

Not only the signal response but also the crushed signal and the M_z response are obtained using the General Electric Signa® Advantage™ EPIC Tool. The final magnetization produced by the crusher pulse is

$$M_{xy}^* = -\beta^2 M_{xy}^{*},$$

and M_z profile is

$$M_z = (\alpha\alpha^* - \beta\beta^*) M_0.$$

The crushed signal response and the M_z profile are given in Figure 3.4.

An important consideration for *in vivo* experiments is the amount of RF power used. Maximum B_1 , the peak RF amplitude required to reach the nominal flip angle, represents a significant power requirement. For a single channel pulse, the flip angle for the center of the slice is given by

$$\theta = \gamma \int B_1(t) dt.$$

When factoring $B_1(t) = B_{1\max} f(t)$, $B_{1\max}$ can be described as ⁷⁴

$$B_{1\max} = \frac{\theta}{\gamma \int f(t) dt},$$

and is directly proportional to the nominal flip angle and inversely proportional to the normalized area under the pulse.

In order to estimate the specific absorption rate (SAR), the integral of the energy delivered during the pulse should be estimated. The energy in [$\text{g}^2 \text{ ms}$] is proportional to

$$E \propto \frac{\theta^2 C}{A^2 pw} ,$$

where θ is the flip angle, pw is the pulse width, and A and C are

$$A = \sum \frac{B_1(i)}{N} ,$$

$$C = \sum \frac{|B_1(i)|^2}{N}$$

where N is the number of points of the digitized pulse.

When the modulation frequencies ν_1 and ν_2 are set to 4.0 and 0.85, the width of the slice of unperturbed spins is 2.5 kHz, while the excitation band is 5.4 kHz in each outer slice for a normalized pulse width of 1 ms. The Bloch simulation indicates this pulse requires a maximum B_1 amplitude of 0.63 gauss at the middle of the pulse, or 1.01 kHz in ^{31}P MR frequency to deliver 90° saturation in the outer region. The relative energy is $0.034 \text{ g}^2 \text{ ms}$.

The cos-sinc pulse has the advantage of saturating both slices at the same time with only real pulse components. It demands higher power capacity to improve ripple in the unperturbed region and to reduce the transition zone by increasing the modulation.

OVS pulse design (II): SLR saturation pulse

Recently Pauly and et .al. demonstrated how to design a pulse that produces a specified slice profile ⁷³ based on the Shinnar-Le Roux (SLR) algorithm which provides the direct solution to the nonlinear Bloch equation^{75,76,77,78}. In the SLR algorithm, the state-space description is reduced to two polynomials using the hard-pulse approximation where the small rotation is modeled by two sequential rotations. The first is free precession under the effect of the local gradient field by an angle $-\gamma G \cdot x \cdot \Delta t$ and the second is the rotation about the applied RF vector by an angle $-\gamma B_1 \cdot \Delta t$. Then the Cayley-Klein parameters at the n^{th} time step are developed and are $(n-1)$ order polynomials.

The General Electric Co. also uses a saturation pulse of linear phase produced by the SLR algorithm. However, since the slice to be saturated will not be refocused, the saturation pulse does not have to have a linear phase. The excited magnetization is to be suppressed by a subsequent dephasing gradient. Therefore, it is advantageous for the excitation pulse to produce the slice with as much phase as possible. This is accomplished by using a maximum-phase pulse, which is based on a minimum-phase $B_n(z)^{73}$.

Using the General Electric Signa® Advantage™ EPIC Tool, the saturation pulse was generated with maximum phase. The bandwidth was set to 2 kHz with a 2 msec pulse width. The bandwidth consists of 0.66 kHz of passband and 1.34 kHz of stopband. The fractional transition band, W , is described in bandwidth as $(1.34 - 0.66)/2 = 0.34$. The pulse profile and its response are shown in Figures 3.5, 3.6 and 3.7.

The Bloch simulation shows the maximum B_1 amplitude is 0.13 gauss at the middle of the pulse to deliver 90° saturation in the passband when the pulsewidth is 2 msec. The relative energy is 0.007 g² ms.

Figures 3.8(a), (b) and (c) illustrate the effects of the maximum phase pulse. Each pulse was simulated based upon the Bloch equation: GE standard 5.8 kHz saturation pulse (SLR-GE), Maximum Phase saturation pulse with 2 kHz bandwidth (SLR-2kHz), and Maximum Phase saturation pulse with 5 kHz bandwidth (SLR-5kHz) in Figure 3.8(a), 3.8(b) and 3.8(c), respectively. The diagrams show the signal, phase, longitudinal magnetization (M_z) and the two transverse magnetizations (M_x and M_y) after a saturation pulse is applied to the initial M_z with no transverse magnetization. The resultant M_z shows the degree of the outer volume saturation. The dispersion of the coherence of the transverse magnetization is shown in M_x and M_y . The degree of dephasing in the saturated region was enhanced by a dephasing gradient right after the saturation pulse (second diagram). The dephasing was substantially improved when the 'SLR-2kHz' saturation pulse was used. When the 'SLR-5kHz' saturation pulse was used, the dephasing was even more enhanced but the resultant magnetization outside of the saturation region had a high and a low frequency modulation. The wider bandwidth pulse also requires more transmitter power. Based upon the Bloch simulations, the Maximum Phase saturation pulse with 2 kHz bandwidth was chosen as an OVS pulse for CSI.

2D OVS/1D ISIS Hybrid

A hybrid pulse sequence was developed which combines OVS and ISIS. Because small changes in position may cause large errors in ISIS, only a one dimensional (1D) ISIS sequence was used. An adiabatic hyperbolic secant selective inversion pulse was used along the surface coil axis where the B_1

gradient is the greatest. The ISIS pulse was positioned after all the suppression pulses.

It is very difficult to calibrate a 90° flip angle for cos-sinc pulse ($B_{1\max}$ of 2.7 kHz) when a surface coil is used. Therefore a train of saturation pulses, as many as required, were employed. Each saturation pulse was followed by a dephasing gradient. After presaturation and the ISIS pulse, the magnetization in the ROI was excited either by a non selective hard pulse or a hyperbolic secant adiabatic pulse. Figure 3.9 shows the hybrid pulse diagram in which double OVS pulses are applied to each direction.

Short T_E Spin Echo

The SPINECHO pulse is the sequence developed by Lim et al.⁷⁹ and adopted in the GE Signa system. The RF pulse pair used is a composite of an initial α pulse followed by a refocusing 180° pulse. Because this pulse produces a spin echo, it avoids the problem of baseline distortion caused by missing data points. The echo time is only 2.5 ms and thus it is barely affected by longer T_2 decay time.

Even though the SPINECHO pulse requires less RF power when compared to self-refocusing pulses, it still requires high level of transmitter power. In this study, the SPINECHO pulse was tested in an attempt to evaluate its application to human ^{31}P MR cardiac spectroscopy.

Spectroscopic Imaging

Even though 3D chemical shift imaging (CSI) is very time consuming, the Fourier spectroscopic imaging method has been used for many localization techniques because spectra are simultaneously obtained from the whole

volume. It would be more efficient to combine CSI with other localization techniques.

The Fourier method gives the best signal-to-noise ratio when a non-selective hard pulse is used. When a slice selective pulse with a single gradient is used, the pulse still gives good signal-to-noise ratio. As described later, the spectroscopic imaging method solved problems that made cardiac spectroscopy almost impossible. First, the excitation pulse before the phase encoding gradient is less prone to power limitation, whereas the π -pulse should be reserved for the ISIS sequence in order to produce quality of localization. Second, the single voxel experiment could not guarantee the specific voxel position which relies on the scout localizer image. There is no way to synchronize the same cardiac phase between two different scan techniques, imaging and spectroscopy. On the other hand, it is easy to shift the spectroscopic grid by multiplying each phase encoded FID by the quantity^{80,81}

$$\exp(-i 2\pi \Delta z \cdot k)$$

where Δz is size of the spectroscopic grid, $k = \gamma \cdot G \cdot t / 2\pi$ and t is the duration of phase encoding. The use of this technique enables the adjustment of the voxel position according to the anatomical requirement⁸².

The most significant problem of the Fourier method is related to the spatial response function which gives the contribution of a point sample to the adjacent CSI voxels. The aliasing problem frequently arises and can be remedied by either shifting the spectral grid or increasing the number of phase encoding steps. It is a trade off between spectral quality and measurement time. Signal bleeding⁸³ is another major problem that arises when the voxel size

is larger than the scale of the biological heterogeneity. In the case of ^{31}P spectroscopy, signal leakage with CSI is not a big problem since phosphorylated metabolites generally have an approximately uniform distribution over the volume elements⁸⁴. For cardiac spectroscopy, the spatial heterogeneity of the heart may be a problem.

The CSI voxel size was limited by the maximum value of the encoding gradient. The field of view is related to the gradient increment:

$$\text{FOV} = 2\pi/\gamma \cdot \Delta G \cdot \tau,$$

where τ is the duration of the phase encoding gradient. The voxel size Δl is related to the maximum value of the encoding gradient ($G_{\max} = (M-1) \cdot \Delta G / 2$).

$$\Delta l = \text{FOV} / M = \pi(M-1) / M \cdot \gamma \cdot G_{\max} \cdot \tau$$

In the CSI experiment in this work, the minimum voxel size was about 1 cm for a 16 voxel 1D CSI.

Several combinations of chemical shift imaging with other localization techniques were tested and are described in Chapter 5. The main scheme for chemical shift imaging was 1D or 2D CSI combined with outer volume presaturation. Figure 3.10 shows the spectroscopic imaging pulse sequence combined with SLR Maximum Phase saturation pulse with 2 kHz bandwidth.

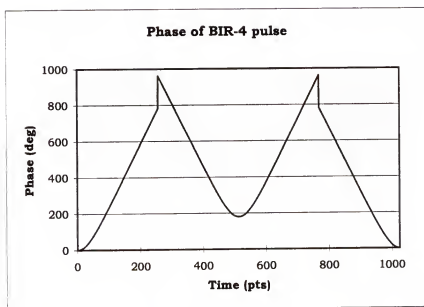
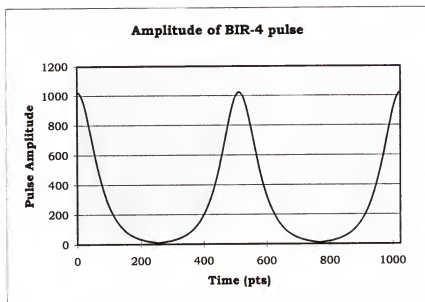


Figure 3.1(a) Phase modulated BIR4 pulse.

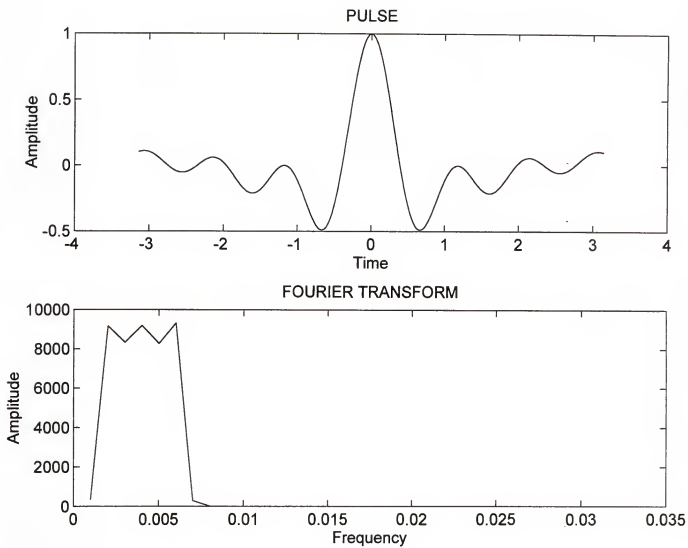


Figure 3.2 Output of the Matlab® pulse generation program.

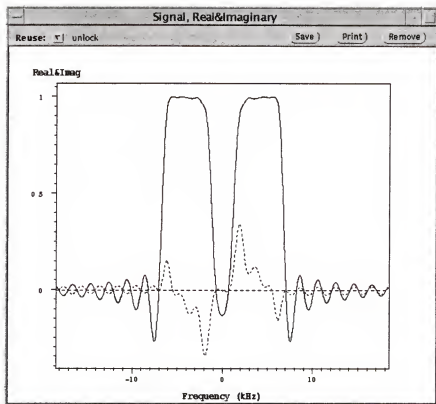


Figure 3.3 Signal response of the cos-sinc pulse.

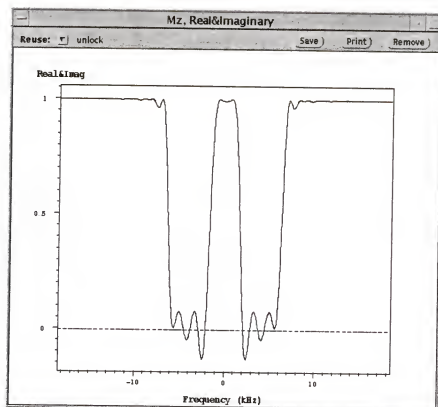


Figure 3.4 M_z response of the cos-sinc pulse.

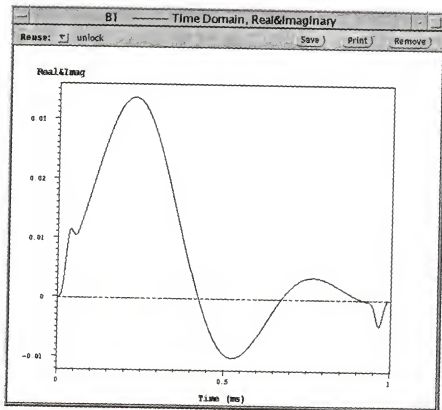


Figure 3.5 Maximum phase SLR saturation pulse.

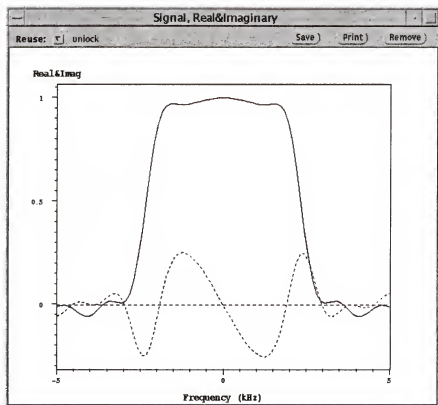


Figure 3.6 Signal response of the SLR saturation pulse.

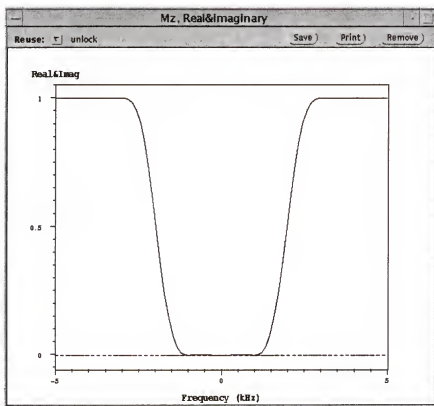


Figure 3.7 M_z response of the SLR saturation pulse.

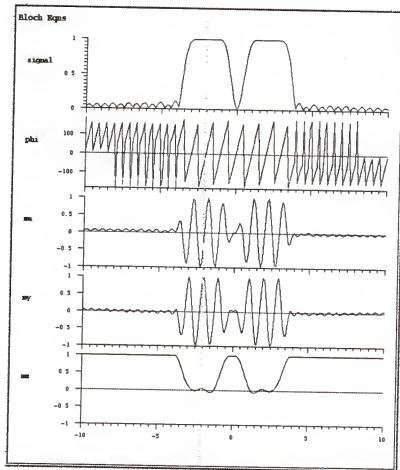


Figure 3.8(a) Bloch simulation of GE standard saturation pulse.

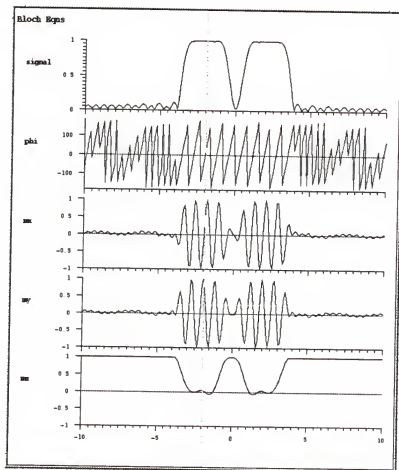


Figure 3.8(a) Bloch simulation of GE standard saturation pulse with dephasing gradient.

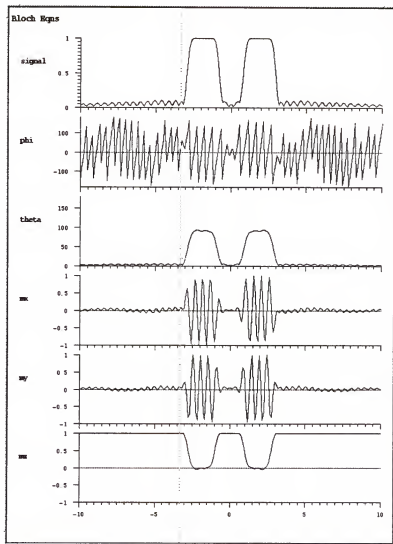


Figure 3.8(b) Bloch simulation of 2 kHz SLR Maximum Phase saturation pulse.

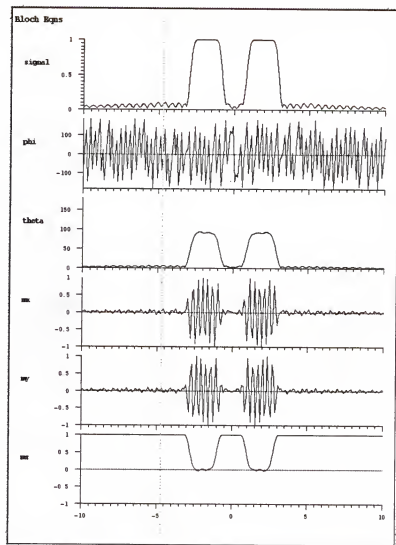


Figure 3.8(b) Bloch simulation of 2 kHz SLR Maximum Phase saturation pulse with dephasing gradient.

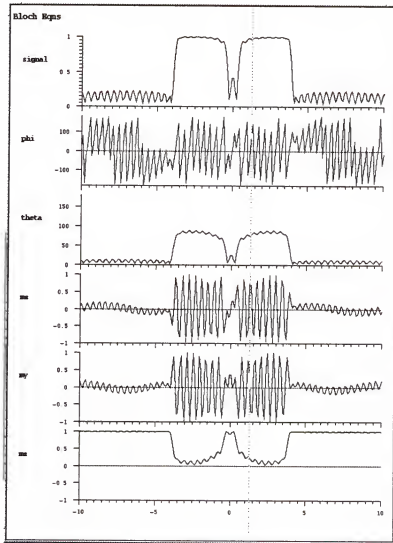


Figure 3.8(c) Bloch simulation of 5 kHz SLR Maximum Phase saturation.

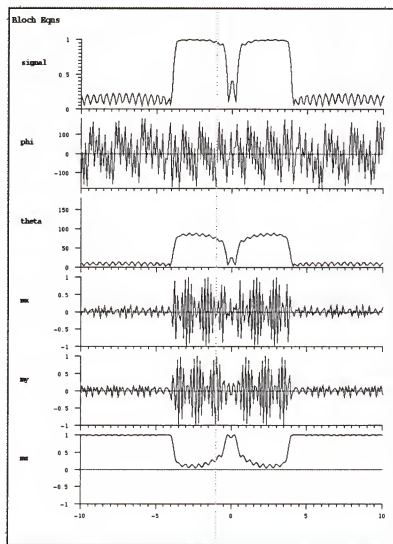


Figure 3.8(c) Bloch simulation of 5 kHz SLR Maximum Phase saturation pulse with dephasing gradient.

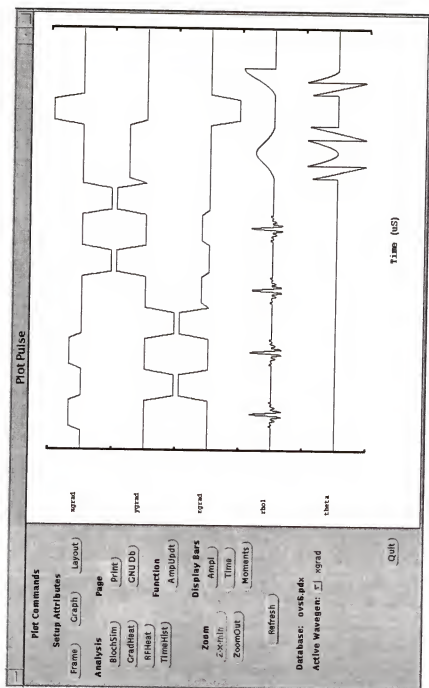


Figure 3.9 Double OVS-ISIS hybrid pulse diagram.

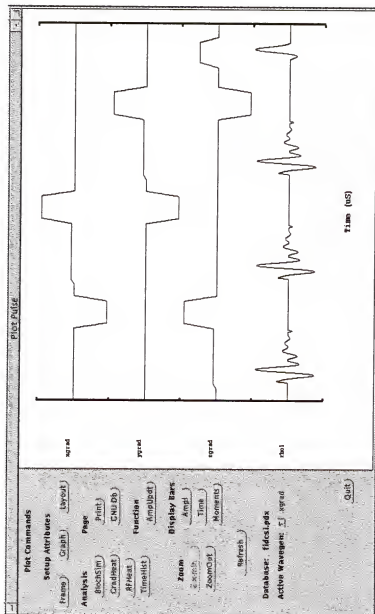


Figure 3.10 CSI combined with SLR Maximum Phase saturation pulse diagram.

CHAPTER 4 MATERIALS AND METHODS

MR System

All MR experiments were conducted with a General Electric 1.5 tesla Signa® Advantage™ whole body imaging system. The host computer on the system is a SUN 3/260. The transceiver processing and storage (TPS) center of the spectrometer consists of its own central processing unit (CPU), an array processor (AP), the excitor, the receiver, the data acquisition board (DAB), the bulk access memory board (BAM), and the integrated pulse generator board (IPG).

In addition to the narrow-band amplifier, standard for normal imaging, there is also a tunable, broadband amplifier, used for spectroscopic data acquisition. Proton spectra are normally acquired using the standard narrow-band amplifier, whereas for ^{31}P experiments a separate T/R (transmit-receive) switch module is attached when the broadband amplifier was used.

Phantom Study

Three phantom sets were built for the purpose of testing the pulses and the pulse sequences.

The first phantom (PHANTOM 1) has two compartments. The 1.5 cm-thick 75 ml inner compartment was positioned in the middle of the large rectangular container of 7 liters (26×32×9 cm). The inner compartment (1.4×4×9 cm), which mimics the heart muscle, was filled with 40 mM methylene

diphosphonic acid (MDPA), and the outer container was filled with 20 mM phosphoric acid (H_3PO_4).

The second phantom (PHANTOM 2) was built in order to test the sensitivity of the instrumentation and the pulses. A 240 mM MDPA solution filled the 12 ml vial, the location of which could be adjusted relative to the bottom of a 6 liter cylinder filled with phosphoric acid. Another phantom (PHANTOM 3) was also built as a complement to test local saturation. It consisted of three compartments: a 3.2 ml innermost cell was filled with 300 mM MDPA which was submerged in the 20 ml vial filled with distilled water. This vial was then positioned in the 0.24 liter bottle filled with 30 mM phosphoric acid. Sodium chloride (70 mM) was added to all the phantoms to make their loading as close as possible to that of the human body. The phantom experiments were designed to be as similar to a human subject as possible.

Figure 4.1 and 4.2 are typical 10 mm slice scout images of PHANTOM 1 and PHANTOM 2. The imaging scan was done by either a spin echo sequence ($T_E = 18$ ms, $T_R = 500$ ms) or a gradient echo sequence ($T_E = 20$ ms, $T_R = 500$ ms, flip angle = 30°). Both phantoms were placed on the 7.5 cm solenoid heart coil. The inductive coupling of the coil interfered, as seen by the darker regions in the bottom of the images.

The voxel or spectroscopic imaging grid was selected based upon these scout images. Then the B_0 field was homogenized by either AUTOSHIM or manual shim using the water peak proton radiofrequency. The STEAM sequence^{85,86} was used to excite and localize the 3 dimensional voxel for the manual shim.

After B_0 shimming was done, the spectrometer was switched to ^{31}P with the ^{31}P T/R switch module. The image obtained in the previous stage was used

as a localizer image in the Scanning Range page. For the single voxel experiment, [Graphic ROI] option was selected and the dimension and position of a voxel were set in the Scanning Range page. For the chemical shift imaging experiment, either [Graphic Rx] option was selected to choose the slices to be scanned, or [Graphic ROI] option was selected to assign the CSI grid.

The phantom studies provided key parameters to be used for *in vivo* study: (1) proper approximate receiver and transmitter gains - R1, R2 and TG for each technique, (2) signal-to-noise figures for each technique corresponding to certain depths, and (3) comparison of the two coils - the transceiver coil (COIL A), and the separate transmit and receive coil assembly (COIL B).

In Vivo Cardiac Spectroscopy

The major differences between the phantom study and the *in vivo* human cardiac study are ECG gating and single voxel shimming.

Human Volunteers

A total number of eight (1 female and 7 male) healthy volunteers were examined in this study. The average age was 32 (from 17 to 42).

ECG Cardiac Gating

All sequences including imaging, shimming and spectroscopy were synchronized with the cardiac pulse using the ECG signal. The gating eliminates or reduces motion effects of the heart. Motion effects in an MR experiment occur whenever a structure moves significantly during the acquisition phase. Cardiac gating depends on the detection of the QRS wave

each time it occurs during a patient's cardiac cycle. The patient is connected to a skin electrode and the cardiac monitor detects the QRS complex and produces a pulse, the R-wave trigger. Triggering is accomplished by detecting the R wave of the ECG waveform after filtering and tailoring of the signal⁸⁷.

The operation is one of threshold detection. The R wave is normally easy to detect. Once the presence of the R wave is established, a variable delay is introduced from detection of the R wave until collecting the data. This delay is adjusted so that the appropriate phase of the cardiac cycle is selected.

In practice, noise may be induced by cable motion or by patient movement. It is very important to reduce the patient-induced noise. The electrode placement is one of the most critical aspects of cardiac gating. In this study, the posterior placement was chosen. Even though anterior placement brings the electrode closer to the heart in patients, this placement can cause an artifact if the ECG cables and the lead wire move up and down through the magnetic field as the patient breathes⁸⁸. Those effects do not occur with a posterior placement. In addition, in this placement it is easier to keep the ECG cables from touching the patient. This protects against false triggering during the acquisitions. Figure 4.3 shows the typical posterior placement of the electrode.

'Auto Lead' was chosen as a trigger lead, which enables the system to detect the absence of signal and looks to another lead with the next highest signal. The gating trigger level was usually chosen to be 65% of full amplitude. The trigger delay between the time the R-wave is detected and the pulse begins is a very important parameter. When it was not properly set, a large noise level was observed. For the series of images, the trigger delay was set at 21 ms as recommended, instead of a minimum delay of about 13 ms. For ³¹P *in vivo* spectroscopy, the trigger delay was set such that the pulse sequence was

positioned half-way between systole and diastole. It varied from 100 ms to 230 ms, depending on the frequency of the heart beat of the human subject.

B₀ Field Shimming

The most significant problem to be addressed in cardiac spectroscopy is signal sensitivity or signal-to-noise ratio. B₀ field inhomogeneity reduces spectral resolution and the signal-to-noise ratio by broadened lines. A better way of obtaining reliable magnetic field (B₀) homogeneity should be provided.

Because the heart is very irregularly shaped and constantly moving, the appropriateness of the conventional methods developed for shimming using localized spectroscopy^{89,90,91,92,93,94} were examined. Pulse techniques such as VSE (Volume Selective Excitation)⁹⁵, developed in the early stages of volume excitation, were excluded because of the high power deposition level. Among commonly used localized spectroscopy, SPARS (SPATIally Resolved Spectroscopy)⁹⁶, was not considered because it has a greater RF load on the patient than STEAM or PRESS, results in significant contamination from outside the VOI, and suffers from T₂ decay due to its long echo time⁹⁷.

In this study, PRESS (Point Resolved Spectroscopy)⁹⁸ and STEAM (STimulated Echo Acquisition Mode)⁹⁹ were considered for the proton MRS technique which would utilize the water signal for homogenization of the B₀ field. PRESS consists of three slice-selective 90°, 180°, 180° RF pulses. The PRESS sequence provides accurate voxel localization and gives a twofold signal-to-noise ratio advantage over STEAM by using a spin echo rather than a stimulated echo. The PRESS technique, however, has long echo times

compared with the STEAM sequence and is less suitable for a fast moving organ like the heart.

Shimming with the STEAM sequence

Because the STEAM sequence has excellent volume definition and short echo time, it is widely used for localized shimming. In this study, the localized volume was prescribed on the axial localizer images using 'Graphic_ROI' which enables graphical prescription of a voxel of interest for STEAM.

The 8 ml voxel ($2 \times 2 \times 2$ cm) was selected which was centered in the left ventricular wall. Cardiac gating was employed to make the pulse synchronized with the ECG pulse. In the 'Manual Prescan' section, the two receiver gains R1 and R2 were set to 7 and 30, respectively. Then the transmitter gain, TG, was determined as the level producing maximum water signal. With the parameters R1, R2 and TG, the water signal was then observed in the 'Single1' entry point. Throughout the shimming process, water suppression pulses were turned off. The primary X-, Y- and Z- gradient current offsets of the shim coil were adjusted until the water signal reached its highest level. To observe the signal intensity, two windows were displayed: one for 'Magnitude Spectrum', which displays the square root of the sum of the squares of the real and imaginary parts of each complex data point in a processed data set, and the other for 'Pure Absorption' which is the real part of the Fourier-transformed data, or the real channel raw FID data.

When the body coil was used as a transmitter and receiver, shimming was very difficult due to the large noise level and fluctuation. Changing the transmitter gain could not deliver significant signal variation with a single scan in 'Manual Prescan' acquisition. Alternatively, the TG level was determined in

the 'average' entry point by averaging 8 or 16 scans. This procedure takes much longer than 'Manual Prescan', however, the signal-to-noise ratio was improved. Moreover, the signal fluctuated significantly due to instrument instability with unknown spikes in the FID during shimming. This fluctuation made it extremely difficult to recognize the response as the shim current levels were adjusted.

These problems can be alleviated by increasing the signal sensitivity. In order to improve proton signal-to-noise ratio, ^1H surface coil spectroscopy was attempted. The RF resonator was doubly tuned to both ^1H and ^{31}P MR frequency. As described in Chapter 2, COIL A was also tuned to the proton frequency using a Schnall type trap circuit. The proton spectrum obtained by a doubly tuned coil is shown in Figure 4.4. The improvement achieved by the surface coil was more significant when it was used for the intact heart than the phantoms.

Shimming with the AUTOSHIM

Since Schneider and Glover developed the rapid *in vivo* proton shimming method¹⁰⁰, it has been adopted as a standard automatic shimming scheme in the GE Signa System. Using the gradient-recalled echo pulse sequence, B_0 homogeneity field maps are generated. The homogeneity map $B_0(x, y)$ is obtained in the form of the phase difference image formed after reconstruction. The fit for only low-order, linear gradients is made with the spatial derivatives of the field. The assumed form of the inhomogeneity is a biquadratic function of the form

$$B_0(x, y) = a_2(x - x_0)^2 + a_1(x - x_0) + b_2(y - y_0)^2 + b_1(y - y_0) + c.$$

The terms a_1 and b_1 determined above represent linear gradients which are to be canceled out. Thus constant correction gradients become,

$$\Delta G_x = -a_1/(\gamma p)$$

$$\Delta G_y = -b_1/(\gamma p)$$

$$\Delta G_{xx} = -a_2/(\gamma p^2)$$

$$\Delta G_{yy} = -b_2/(\gamma p^2)$$

where p is the pixel size.

In the cardiac study, this sequence - two interleaved acquisitions - was tested for the thoracic cavity including the heart and chest muscle. The question was whether this sequence would be appropriate for the B_0 field homogenization for the moving heart. If this rapid shimming scheme is suitable, it would save time, because the linear shim adjustment can be done for all three axes at the same. Moreover, when a region of interest contains the local region around the left ventricles, localized shimming would be possible by deriving the local shim values for a small region in the vicinity of the anterior myocardium.

The proton signal was obtained from an 8 ml voxel by the STEAM sequence after AUTOSHIM was applied. It was evident that global shimming over the entire axial field-of-view did not improve the B_0 field homogeneity substantially. When the local shim was employed over a smaller region including the anterior myocardium and adjacent chest muscle, a significant improvement of magnetic field homogeneity was achievable. From the localizer image, AUTOSHIM can be done either for global shim or localized shim by assigning the region-of-interest over the desired part of the axial image. The B_0 maps in the 3 axes were displayed for both the global and zoomed ROI. Figure

4.5 shows the proton spectrum obtained by the STEAM sequence after localized (zoomed) AUTOSHIM. The AUTOSHIM provided very reliable shim capability without any time consuming manual iteration for the linear shim values. Compared to the manual shim procedure, the AUTOSHIM showed superior line width even though it was done without any cardiac synchronization.

In Vivo Spectroscopy Protocol

Both the manual shim and the AUTOSHIM can be applied for B_0 field shimming. Even though the AUTOSHIM using gradient-recalled echo pulses does not utilize cardiac gating, this fast automated shimming method showed superior shim capability in human subjects. Therefore, the AUTOSHIM was used to homogenize the B_0 field locally.

The other parameters (TG, R1, R2, etc.) determined in the phantom study were used.

1. Patient preparation: Place ECG electrodes on the patient's back as shown in Figure 4.3. Position is 'Feet First' and 'Supine'. Mark on the lower two third of the sternum (Mark#1)¹⁰¹. This mark will be referenced to the second image.
2. Imaging 1: Landmark on Mark#1. Scan axial. FOV=40 cm, Slice thickness = 10 mm, Scan range = I50.0 - S50.0, Cardiac Gating, recommended trigger delay, $T_R = 2 \text{ RR}$, Spin Echo $T_E=27 \text{ ms}$. After scanning, select the slice which shows the myocardium of the anterior left ventricle at its thickest and closest to the chest wall.
3. Coil placement: From the image, measure the relative distance from Mark#1 to the anterior myocardium to be localized. Mark the new

- point according to the measurement from the image (Mark#2). Place the heart coil such that the coil center is positioned at Mark#2.
4. Imaging 2 (optional): Landmark on Mark#2. Scan with the same parameters as in step 2. Check the center slice. If the slice is not far off, proceed to step 5.
 5. AUTOSHIM: Scan plane is axial. In the 'Gradient Shim' page, reset all three linear gradient shim values. With the localizer axial image that was reconstructed from the 'Exec Autoshim', either choose shimming over the entire scan plane first, or directly select localized shim. Choose the ROI about 10 cm in diameter over the region including the myocardium in the anterior left ventricle and overlying chest skeletal muscle. Run the AUTOSHIM procedure in all three planes, over the selected ROI region, select [3-Plane Calc]/[Exec Autoshim]. Then the system runs two more scans centered on the cursor, displays the B_0 map and calculates the fitting parameter. Check that the X^2 , Y^2 and Z^2 coefficients are within ± 0.3 . Check that the water signal from an 8 ml ($20 \times 20 \times 20$ mm³) voxel using the gated STEAM sequence has satisfactory line width and line shape for spectroscopy.
 6. Manual Shimming (optional): In the gated STEAM sequence, select option [Graphic Prescription 3D/ROI]. Determine an 8 ml ($20 \times 20 \times 20$ mm³) voxel in the anterior myocardium, with the caution not to include any chest muscle. $T_R = 2$ sec, NEX = 1 or 2. FOV = 24, [Start Single] in the Spectroscopy page. Set transmitter gain (TG) value by maximizing the water peak from the heart. Adjust X-, Y- and Z- shim values to maximize the water signal. Save the shim values.
 7. ^1H to ^{31}P spectroscopy: Attach ^{31}P T/R switch module. Do (a) single voxel experiment (OVS-ISIS), or (b) CSI (ISIS-CSI, or DRESS-CSI).

7-1 Single voxel experiment (OVS-ISIS):

Scan plane = axial, Spectral width = 2000 Hz, ISIS_CYCLE=2.
ECG gating, Auto Lead, 3 RR, Trigger delay = 100 ~ 200 ms, Even
Spacing ISD(*Inter-Sequence Delay*). Make a voxel on the axial
image: FOV = 25, voxel size = 15x20x20. Number of saturation
pulse = 3, NEX = 512. Average in 'avg' entry point, or [Scan].

7-2 CSI experiment (2D ISIS- 1D CSI):

Scan plane = coronal, Spectral width = 2000 Hz, ISIS_CYCLE =4,
ECG gating option, Auto Lead, 3 RR, Trigger delay = 100 ~ 200
ms, Even Spacing ISD. AP CSI resolution = 8 or 16, Make a voxel
manually from the values on the Review Screen, NEX=64. [Scan].



Figure 4.1 10 mm slice axial image of PHANTOM 1.



Figure 4.2 10 mm slice axial image of PHANTOM 2.



Figure 4.3 Typical posterior placement of the ECG electrode.

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000000333
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SW : 1000.0
SIZE : 1024
PNTS : 1 to 1024
LINES : 1 to 1
CHAN : 1

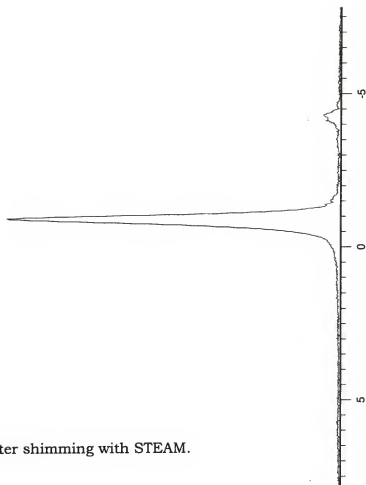


Figure 4.4 Proton spectrum after shimming with STEAM.

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000970408
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PNTS : 1 to 1024
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CHAN : 1

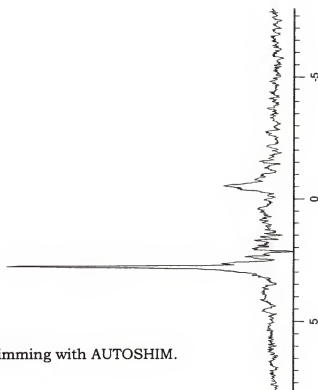


Figure 4.5 Proton spectrum with B_0 shimming with AUTOSHIM.

CHAPTER 5 RESULTS AND DISCUSSION

Phantom Experiments

Tests of the Coils

The quality and characteristics of the two types of surface coils were measured in terms of B_1 field strength and the change of the field magnitude. From the practical point of view, the signal from the region where the myocardium was mimicked was traced as a function of transmitter gain. The surrounding medium was regarded as a component surrounding the region-of-interest. The signals were measured from the single slice in the middle of which there was the inner compartment filled with MDPA surrounded by phosphoric acid (H_3PO_4).

COIL A

A typical ^{31}P spectrum containing the MDPA triplet and phosphoric acid peak from PHANTOM 2 is given in Figure 5.1. Figures 5.2(a) ~ 5.2(d) show the MDPA and H_3PO_4 signal from PHANTOM 2 obtained using the 7.5 cm tranceiver coil (COIL A). When the 50 mm deep, 25 mm thick - coronal slice was scanned, the transmitter gain which produced the maximum signal intensity was 140 with a 1.8 ms slice selective pulse (Figure 5.2(a)). The same slice delivered the same signal intensity with a 3.6 ms pulse, whereas the transmitter gain for maximum signal intensity was reduced by 3 dB (Figure 5.2(b)). This reduction

of TG value was possible by increasing the amplitude of the slice selective pulse which had been automatically reduced as the pulse width increased to 3.6 ms. The amplitude of the pulse was maximized by setting the control variable 'a_rf1' to 0.95.

When the axial slice was excited, the signal intensity of the two phosphate peaks changed as B_1 field varied with TG over 70 as shown in Figure 5.2(c) and (d). A longer slice selective pulse (3.6 ms) was chosen to reduce the thickness of the slice down to 20 mm. The signal changes corresponding to the TG variation were similar for both normal amplitude (a_rf1=0.438) and maximum amplitude (a_rf1=0.95) of the excitation pulse. As shown in Figure 5.2(a) to (d), the signal from the surroundings around the region-of-interest (ROI) obtained by COIL A showed sharp variation depending on the transmitter power level. This steep variation made it very difficult to calibrate the pulse which delivers the RF power at an optimized level. Pulses such as the outer volume presaturation pulse can not be employed successfully unless the transmitter gain is optimally calibrated.

COIL B

A similar scan was done using the separate transmit-receive COIL B. Figures 5.3(a) ~ (e) show the spectra obtained from the same PHANTOM 2. Whatever slice was scanned, the signal amplitude did not vary over a wide range. Once the transmitter gain was above the certain level, the signal intensities, whether from a layer deep inside the phantom or from the surroundings, maintained their levels. This invariability was maintained regardless whether the scan plane was axial or coronal, the pulse width/slice

thickness were varied from 1.8 ms pulse for 25 mm slice to 3.6 ms pulse for 20 mm slice, or pulse heights were high or low.

Therefore, COIL B was more suitable when it was used with the outer volume presaturation, because it had less susceptibility to the transmitter power level. Whereas COIL A suffered from significant signal variance.

The signal-to-noise ratios (SNR) of the two coils showed comparable values. COIL B showed a slightly better signal-to-noise figure. The signal-to-noise ratios are shown in Table 5.1. All the signal was obtained by 16 scan-average and TG values were adjusted to maximize the signal.

Table 5.1 SNR comparison from MDPA peak between the two coils

	a	b	c	d
Coil A	16.01	10.37	9.42	9.12
TG	140	100	150	90
Coil B	17.09	9.97	11.74	11.41
TG	200	185	195	170

a) 25mm coronal slice with 1.8 ms pulse ($a_{rf1}=0.44$)

b) 20mm coronal slice with 3.6 ms pulse ($a_{rf1}=0.88$)*

c) 20mm axial slice with 3.6 ms pulse ($a_{rf1}=0.44$)

d) 20mm axial slice with 3.6 ms pulse ($a_{rf1}=0.88$)*

* The amplitude control value (CV) of the excitation pulse, ' a_{rf1} ' was doubled which controls the amplitude of the pulse out of the pulse generator.

If the larger transmitter of COIL B is assumed to deliver uniform B_1 field over the sample volume, this uniform flip angle produces increased penetration

depth relative to COIL A. In the homogeneous excitation experiment, 90% of the total signal is obtained from the sample volume located within 2.8 radii of the coil plane, whereas for the single-coil experiment 90% of the signal is obtained within a depth of one radius¹⁰². However, signal cancellation due to phase mismatches between the transmitter and the receiver occurred in the case of COIL B. The total signal intensities for the two experiments are expected to be similar for a single pulse at equilibrium¹⁰³, which agrees with the results obtained.

Despite all the advantages of COIL B, it required more power than COIL A due to its large transmitter coil size. In summary, COIL A and COIL B showed comparable signal-to-noise ratio in a well defined region. COIL B delivered a more homogeneous B_1 field over the entire region sensitive to the receiver coil. COIL A could be driven by smaller transmitter power, but gave a less homogeneous B_1 field.

Short T_E Spin Echo Pulse

The self-refocused spin echo RF pulse pair was tested using both coils. In most cases, the power level was the limiting factor even though the pulse adopted in the GE Signa® system requires less power than other self refocusing ones¹⁰⁴. The MDPA signal level had never been significant when COIL A was used and an axial slice was excited (Figure 5.4(a)). In the coronal slice excitation, the MDPA peak was observed and had an increased magnitude, but it did not reach its optimum level even with the highest transmitter gain (Figure 5.4(b)). As the B_1 field increased, not only did both signals increase (Figure 5.4(c)) but the noise level increased as well such that

the SNR of MDPa peak was 11.2 and 8.9 for TG of 150 and 200, respectively. COIL B did not show reasonable MDPa peaks with the SPINECHO pulse, but only noisy and insignificant ones. For both coils, the self-refocused spin echo pulse could not be used for deep seated regions ($\geq 5\text{cm}$).

OVS-ISIS Localization

Figure 5.5(a) shows the unlocalized phosphorus spectrum obtained with COIL A from PHANTOM 2. COIL A was placed on the bottom of the 7 liter container phantom. The phosphoric acid peak is much larger than the MDPa peak.

When the saturation pulse was employed with the gradient in the X and Z directions, the phosphoric acid signal was suppressed. Even though the outer volume presaturation was implemented successfully in the slice parallel to the coil plane, it was not possible to achieve perfect presaturation in the direction of the coil axis. The B_1 field intensity was rapidly falling off as the distance from the coil increased. Therefore, it is impossible to saturate the entire region between the coil and the voxel in the ROI. Figure 5.5(b) illustrates the imperfect localization when localization was attempted with presaturation pulses along all three dimensions.

As indicated in the previous chapter, the B_1 insensitive adiabatic pulse can solve the problem of a severe B_1 field gradient. However, it is very time consuming to calibrate the power level of the 90° saturation for different depths. The B_1 field varies even in a given slice of the subject. Moreover, the surface coil is positioned on the chest, where, in most cases, the coil plane is not aligned with the Cartesian coordinates. This results in a mismatch or

asymmetry between the relative coil orientation and the selected plane which is determined by X, Y and Z directions. It is very difficult to attain a 90° pulse in the entire plane to be suppressed, because the distance from the coil center to both ends of the voxel is not the same when the coil is not positioned exactly horizontally.

This situation was alleviated by using more than one set of saturation pulses in series. As the number of the saturation pulses increased, the outer volume suppression improved. With only a single set of saturation pulses in each direction, there remains a significant amount of signal from outside of the voxel, as shown in Figure 5.5 (c). When three consecutive sets of pulses are applied with a dephasing gradient, the outer volume signal from a 3.5 cm deep slice was completely suppressed, as shown in Figure 5.5 (d).

Spectroscopic Imaging I.

For deep-seated cardiac ^{31}P spectroscopy, chemical shift imaging was implemented with several variations.

First, simple one dimensional chemical shift imaging was done for PHANTOM 1. Phosphoric acid gives a dominant signal which is modulated in the phase encoding direction Y (Figure 5.6). When it was combined with the 3D ISIS sequence which defined a 1.5 x 3.0 x 2.0 cm voxel, the MDPA peak was well defined in the fourth CSI voxel (Figure 5.7 (a)). However, the sequence combined with 3D ISIS could not be used for cardiac spectroscopy. For 2D ISIS with a 1.5 x 3.0 cm column, the surrounding phosphoric acid gives spatial signal strength variation (Figure 5.7 (b)). In this experiment, the ISIS column was in the Z and CSI phase encoding was in the Y direction. These prescriptions were made by an axial localizer image.

After switching the localizer image to a coronal slice, the ISIS column was in the Y direction, which was the same as the coil axis. This gave good spatial localization and spatial distribution of the spectra (Figure 5.8).

Another CSI scheme was tested using the DRESS sequence. Using the XY plane scout image, the phantom was excited by depth resolved excitation followed by phase encoding in the Y direction (Figure 5.9). The depth resolved pulse does not show a perfect slice selection such that the signals coming from the outside of the slice (4th and 5th CSI spectra) were observed in the other CSI spectra. In addition, the DRESS sequence could not eliminate the surrounding volume which was in the plane excited by the RF pulse.

Various CSI combinations with proper localization can provide unique features that are not available with single voxel spectroscopy. For the purpose of cardiac spectroscopy, 1D CSI coupled with 2D ISIS shows strong potential.

Spectroscopic Imaging II.

As stated in the previous section, chemical shift imaging combined with ISIS gave good spatial localization for the phantom study. However, when these sequences were applied to the human heart, several critical problems appeared.

One problem was that the localization quality depends on the spin-lattice relaxation (T_1) time. For heart muscle, the ^{31}P spin-lattice relaxation times are reported to vary from 4.1 to 5.3 sec for PCr and from 1.7 to 2.6 sec for ATP^{105,106,107,108,109} in 1.5 tesla systems. Because for ISIS the longitudinal magnetization is inverted by sequential permutation of alternating π pulses, the repetition time (T_R) should be longer than $3 T_1$. A repetition time longer than 15 sec is not practical for low sensitivity ^{31}P cardiac MR spectroscopy. The other

problem was that the spectra using the ISIS sequence were severely compromised by motion. Motion artifacts are inevitable for cardiac spectroscopy. These problems are much more severe for 2D or 3D ISIS where previously inverted magnetization is subsequently inverted with another directional gradient. Therefore 1D CSI coupled with 2D ISIS was discarded as a possible option for cardiac spectroscopy.

The spectroscopic imaging method combined with outer volume presaturation could alleviate the aforementioned problems. One- and two-dimensional chemical shift imaging combined with SLR presaturation pulses were tested. The new SLR saturation pulse as described in Chapter 3 was combined with one or two dimensional CSI. In the 1D CSI experiment, two dimensional volume suppression was done by presaturation pulses in the right/left and superior/inferior directions. The SRL pulse was processed by Hadamard encoding to make double sided saturation for 1D CSI. When the overlying chest skeletal muscle was saturated, only a single slice over the heart was suppressed using the newly designed maximum phase saturation pulse.

Figures 5.10(a) - (d) show the result from PHANTOM 2 scanned by 2D CSI in the XZ (coronal) plane using COIL A. In the plane, spatial localization was done by chemical shift imaging. The XZ plane was selected with a DRESS-like slice selective pulse, and the volume underneath of the plane was presaturated. The spectrum from the voxel positioned at the center of MDPa bottle shows a high degree of the localization (Figure 5.10(a)). The spectra changed along the voxels in the X (Figure 5.10(b)) or Z (Figure 5.10(c)) directions. Figure 5.10(d) illustrates spectra from the voxel containing the MDPa bottle and surrounding voxels.

When the XY (axial) plane was scanned, similar quality of localization was obtained. Figure 5.11 shows Y directional CSI spectra using COIL B where the volume in the X and Z directions was presaturated.

Human *in Vivo* Cardiac Spectroscopy

^{31}P MR Cardiac Spectra

The 2D OVS/1D ISIS hybrid sequence and CSI sequence were used to obtain ^{31}P spectra from the heart.

Figure 5.12(a) and (b) shows two ^{31}P spectra from the myocardium of a healthy volunteers using the 2D OVS/1D ISIS hybrid technique and ECG cardiac gating. B_0 field was homogenized by manual shimming using the STEAM sequence. The spectrum from the chest muscle overlying the heart obtained from the same volunteer is shown in Figure 5.12(c). Spectrum 5.12(a) was obtained with a single OVS pulse and 5.12(b) with three pulses. The scan was done with repetition time at every 3 R-R beats. The peaks of 2,3-DPG at about 5.4 ppm and 6.3 ppm overlapping Pi indicate contamination from the blood in the chamber.

Four spectra were obtained from other healthy volunteers using CSI/OVS. Since this Fourier method excited volume elements in the given slices simultaneously, the spectrum from the overlying heart muscle was also obtained at the same time. To avoid time consuming 3D CSI, a single slice was excited before phase encoding. When anterior-posterior 1D CSI was done on the axial plane, OVS pulses were applied to the X (left-right) and Z (anterior-posterior) directions. The 2D CSI was done on a coronal slice with an OVS

pulse applied to the chest muscle. Before the MR frequency was switched from ^1H to ^{31}P , localized or zoomed AUTOSHIM was used to homogenize the B_0 field over the anterior left ventricle. The acquisition was completed with 512 scans. Thus the number of excitations (NEX) for each of the 16 phase encoding steps in the 1D CSI was 32. Each 8×8 2D CSI used 8 NEX. The repetition time (T_R) was set to 3 R-R wave intervals.

Figure 5.13(a) shows one of the CSI spectra from the heart. The fifth spectrum in Figure 5.13(b) is a ^{31}P spectrum from the left ventricular anterior myocardium. The third spectrum in the same CSI spectra is the one from the chest muscle (Figure 5.13(c)). Figure 5.13(d) is the same suite of CSI spectra as Figure 5.13(a) but the phase was changed to make the third spectrum an absorption mode. These examinations generally took 25 minutes to complete 512 CSI scans.

PCr/ATP Ratio

Table 5-2 shows the relative PCr peak areas normalized to the α -ATP obtained from seven healthy volunteers. Because the γ -ATP peak was not well separated from PCr in the spectra, and the β -ATP peak was sometimes broadened by variation of pulses, the α -ATP peak area was used as the normalization factor.

The FID data was filtered by 10 Hz exponential line broadening. The first order and zero order phase was corrected on the frequency domain phosphorus spectrum after Fourier transformation of the time domain FID data set. The baseline of the spectrum was corrected by a cubic spline. Then each metabolite peak was identified and the Gaussian fitting was done using a Marquardt-

Levenberg fitting function. The Gaussian line shape was selected because of the peak shape of the spectra.

Table 5.2 Partly saturated PCr/ATP ratio from human heart muscle

Volunteer	A	B	C	D	E	Average
TR	3RR	4RR	3RR	3RR	3RR	
technique	2D OVS/ISIS	OVS/1D CSI	OVS/1D CSI	OVS/2D CSI	OVS/1D CSI	
PCr/ATP	0.99	1.06	1.41	1.42	1.17	1.21±0.19

The PCr/ATP ratio is an important index of energy metabolism. The mean PCr/ATP ratio of the heart muscle was 1.21 ± 0.19 , whereas the PCr/ATP ratio of overlying skeletal muscle in an adjacent voxel (possibly a mixture of heart and muscle) was 2.43 ± 0.75 (Table 5.3).

Table 5.3 Partly saturated PCr/ATP ratio from a voxel adjacent/exterior to the heart layer

Volunteer	A	B	C	D	E	Average
PCr/ATP	2.38	3.61	2.25	2.38	1.52	2.43 ± 0.75

All the spectra except volunteer B were obtained with 3 R-R interval repetition time. The T_R of volunteer B was 4 R-R. The PCr/ATP ratios of the myocardium were obtained from the partially saturated spectra, since the T_R time of 3 R-R is about 3 seconds which is too short for longitudinal magnetization to be completely relaxed when the T_R is compared with the spin-

lattice relaxation time of PCr and ATP. The differences in the T_1 values of the two metabolites gives an incorrect PCr/ATP ratio without any T_1 adjustment.

Published metabolite T_1 data^{110,111,112,113,114,115} for the human heart vary considerably. The mean ratio of T_1 is 1.9 ± 0.3 with $T_1(\text{PCr}) = 4.4 \pm 0.5$ and $T_1(\text{ATP}) = 2.4 \pm 0.4$ seconds¹¹⁶. Using the above T_1 value, the saturation factor is about 1.3 when the repetition time (T_R) is 3 second, and a 60° flip angle is used.

A better approach would be to measure the saturation factor directly from the ratio of spectra acquired under both partially saturated and fully relaxed conditions. In this study, two scans were added after the localized spectroscopy. One spectrum was obtained under partially saturated conditions with a T_R of 2 to 3 seconds. The other was obtained under fully relaxed conditions with a T_R of 15 seconds for volunteers A and E. Those two additional measurements used a 0.5 ms hard pulse. The use of this non-selective hard pulse relied on the assumption that the T_1 ratio of PCr to ATP in the myocardium is not substantially different from the T_1 ratio in all tissues that contributed to the unlocalized surface coil spectrum¹¹⁷. Support for this assumption is provided directly by some T_1 measurements of skeletal and heart muscle and by measurements of saturation factors as a function of the fraction of chest muscle contributing to the unlocalized spectrum¹¹⁵.

Table 5.4 Partial saturation correction factors

Volunteer	A	E
(a) PCr/ATP ($T_R=15$ s)	7.01	3.27
(b) PCr/ATP ($T_R= 3$ s)	5.43	2.92
(a) / (b)	1.3	1.1

Using these adjusting factors, the myocardial PCr/ATP ratio was corrected to 1.5 ± 0.3 . The saturation factors are all 1.3 except for volunteer E. In a future study, the reproducibility of measured saturation factors could be examined.

Table 5.5 PCr/ATP ratio adjusted by saturation correction factors

	A	B	C	D	E	Average
PCr/ATP (no correction)	0.99	1.06	1.41	1.42	1.17	1.21
Saturation Factor	1.3	1.3	1.3	1.3	1.1	
PCr/ATP (corrected)	1.277	1.378	1.833	1.846	1.315	1.53

Blood Contamination

Peaks at 5 to 6.5 ppm downfield from the PCr were observed. These peaks were partly from the blood which contains 2,3-DPG, producing a doublet at 5.4 and 6.3 ppm, near inorganic phosphate and other phosphomonoester resonances. The blood contains ATP but not PCr¹¹⁶ and it results in an apparent reduction in the observed myocardial PCr/ATP ratio. The amount of ATP added by blood can be estimated from the known ratio of $[ATP]/[DPG] = 0.30 \pm 0.02^{118,119,120}$. The measurement of 2,3-DPG in the contaminated spectrum could be used for correction of ATP such as:

$$\text{True [ATP]} = \text{Contaminated [ATP]} - 0.15 \cdot [2,3\text{-DPG}]$$

The overlapping the 2,3-DPG resonance over the Pi region was hard to measure. It has been reported that blood contamination typically increases PCr/ATP values by $13\% \pm 6$ ^{121,122}. Correction for this blood contamination would increase the PCr/ATP ratio from 1.63 to 1.82.

FILE : G00044.001.000
 000970429
 DATE : May 8 18:49:55 1997
 CF : 25.87 MHz
 SW : 2000.0
 SIZE : 2048
 PNTS : 357 to 1381
 LINES : 1 to 1
 CHAN : 1

82

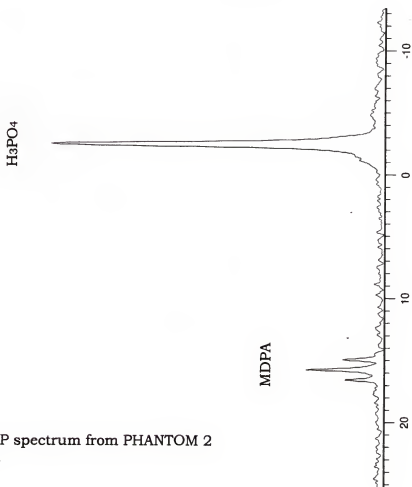


Figure 5.1 Unlocalized ^{31}P spectrum from PHANTOM 2 using COIL B.

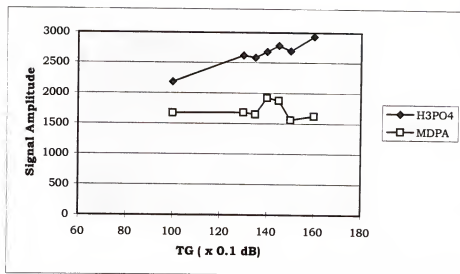


Figure 5.2(a) Signal from the 5 cm deep 25 mm coronal slice with a 1.8 ms excitation pulse using 7.5 cm transceiver COIL A.

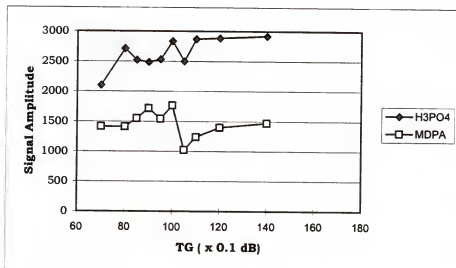


Figure 5.2(b) Signal from the 5 cm deep 20 mm coronal slice with a double amplitude 3.6 ms excitation pulse using COIL A.

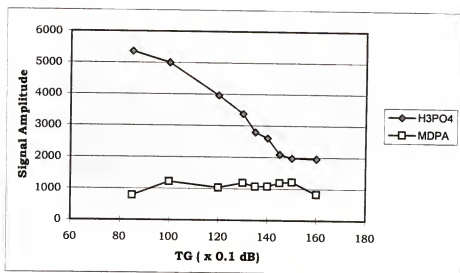


Figure 5.2(c) Signal from the 5 cm deep 20 mm axial slice with a 3.6 ms excitation pulse using COIL A.

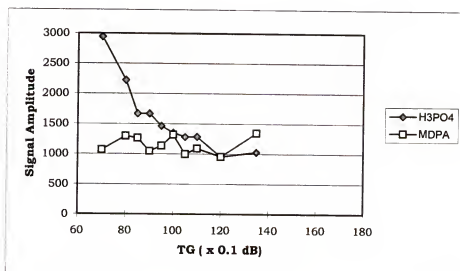


Figure 5.2(d) Signal from the 5 cm deep 20 mm axial slice with a double amplitude 3.6 ms excitation pulse using COIL A.

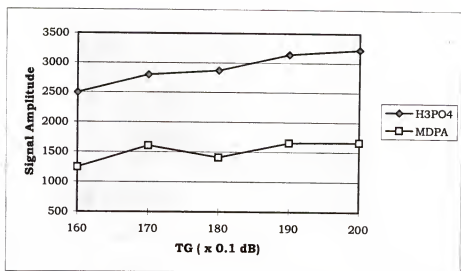


Figure 5.3(a) Signal from the 5 cm deep 25 mm coronal slice with a 1.8 ms excitation pulse using separate transmitter/receiver COIL B.

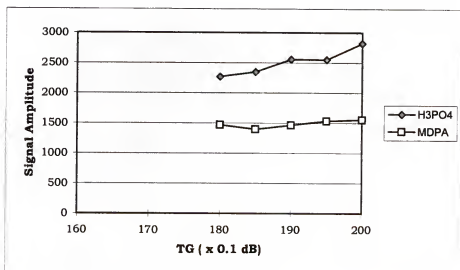


Figure 5.3(b) Signal from the 5 cm deep 20 mm coronal slice with a 3.6 ms excitation pulse using COIL B.

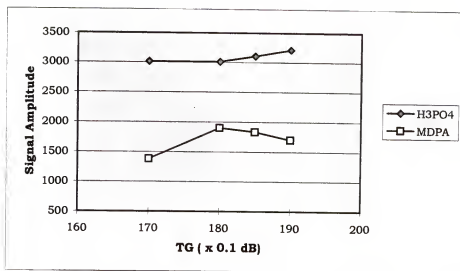


Figure 5.3(c) Signal from the 5 cm deep 20 mm coronal slice with a double amplitude 3.6 ms excitation pulse using COIL B.

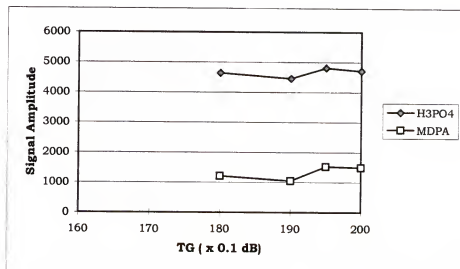


Figure 5.3(d) Signal from the 5 cm deep 20 mm axial slice with a 3.6 ms excitation pulse using COIL B.

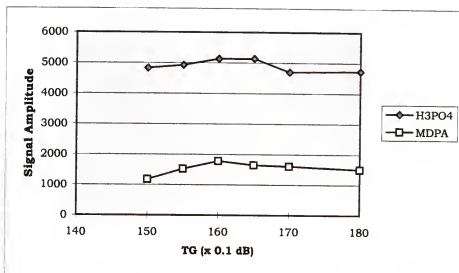


Figure 5.3(e) Signal from the 5 cm deep 20 mm axial slice with a double amplitude 3.6 ms excitation pulse using COIL B.

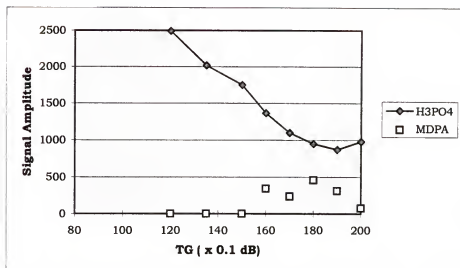


Figure 5.4(a) Signal from the 5 cm deep 20 mm axial slice with the SPINECHO pulse using 7.5 cm transceiver COIL A.

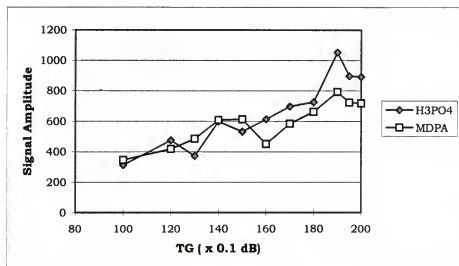


Figure 5.4(b) Signal from the 5 cm deep 20 mm coronal slice with the SPINECHO pulse using COIL A.

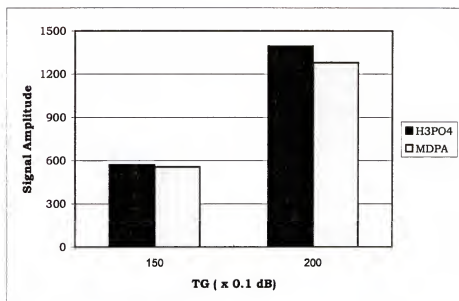


Figure 5.4(c) Signal intensity changes depending on the transmitter gain TG = 150/200 from the 5 cm deep 20 mm coronal slice with the SPINECHO pulse using COIL A.

FILE : G01427.001.000
000000111
DATE : Jun 7 23:56:00 1997
CF : 25.87 MHz
SW : 2000.0
SIZE : 2048
PNTS : 1 to 2048
LINES : 1 to 1
CHAN : 1

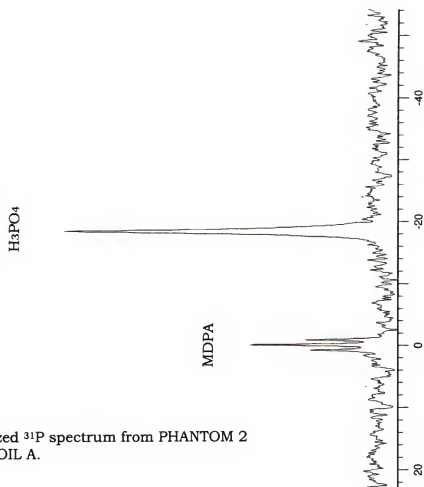


Figure 5.5(a) Unlocalized ^{31}P spectrum from PHANTOM 2 using COIL A.

FILE : G01430.001.000
000000111
DATE : Jun 8 00:03:39 1997
CF : 25.87 MHz
SW : 2000.0
SIZE : 2048
PNTS : 1 to 2048
LINES : 1 to 1
CHAN : 1

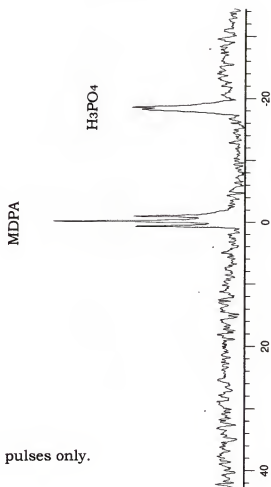


Figure 5.5(b) ^{31}P spectrum localized by OVS pulses only.

FILE : G01432.001.000
000000111
DATE : Jun 8 00:42:17 1997
CF : 25.87 MHz
SW : 4000.0
SIZE : 4096
PNTS : 1372 to 3420
LINES : 1 to 1
CHAN : 1

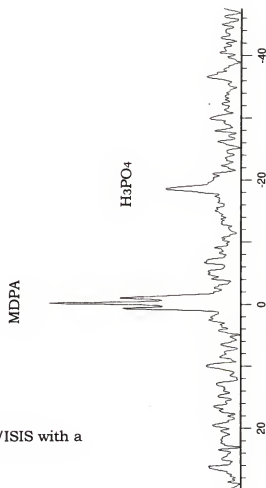


Figure 5.5(c) ^{31}P spectrum localized by OVS/ISIS with a single saturation pulse.

FILE : G01431.001.000
000000111
DATE : Jun 8 00:42:34 1997
CF : 25.87 MHz
SW : 4000.0
SIZE : 4096
PNTS : 1372 to 3420
LINES : 1 to 1
CHAN : 1

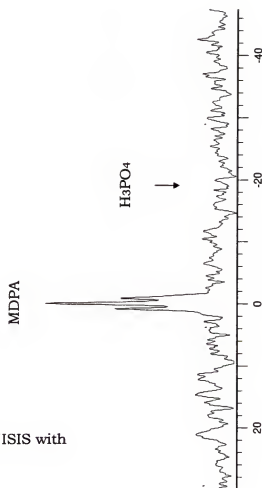
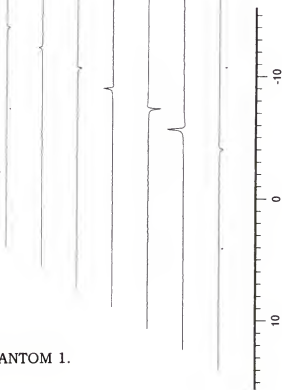


Figure 5.5(d) ^{31}P spectrum localized by OVS/ISIS with three saturation pulses.

FILE : P00000.I-1-2-3
 -4-5-6-7-8
 DATE : Mar 1 14:11:54 1997
 CF : 63.85 MHz
 SW : 2000.0
 SIZE : 2048 x 8
 PNTS : 1 to 2048
 LINES : 1 to 8
 CHAN : 1

94



Phase Encoding
 Direction
 ↑

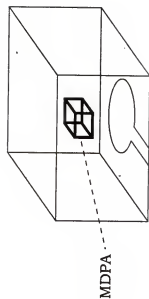


Figure 5.6 1D CSI ^{31}P spectra from PHANTOM 1.

FILE : P34816.1-2-3-4
 -5-6-7-8-9
 DATE : Mar 1 14:16:32 1997
 CF : 63.90 MHz
 SW : 2000.0
 SIZE : 2048 x 8
 PNTS : 1 to 2048
 LINES : 1 to 8
 CHAN : 1

95

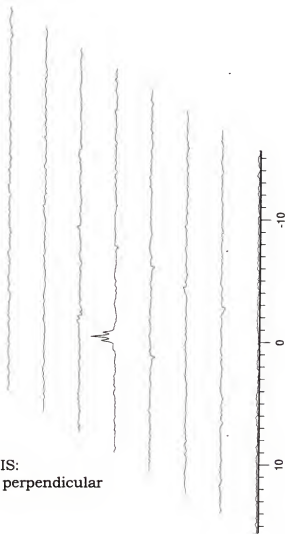
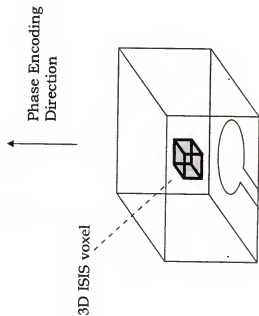


Figure 5.7(a)

^{31}P spectra by 1D CSI/3D ISIS:
 Phase encoding direction is perpendicular
 to the surface coil plane.

FILE : P00512.1-2-3-4
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 DATE : Mar 1 14:02:38 1997
 CF : 63.85 MHz
 SW : 2000.0
 SIZE : 2048 x 8
 PNTS : 1 to 2048
 LINES : 1 to 8
 CHAN : 1

96

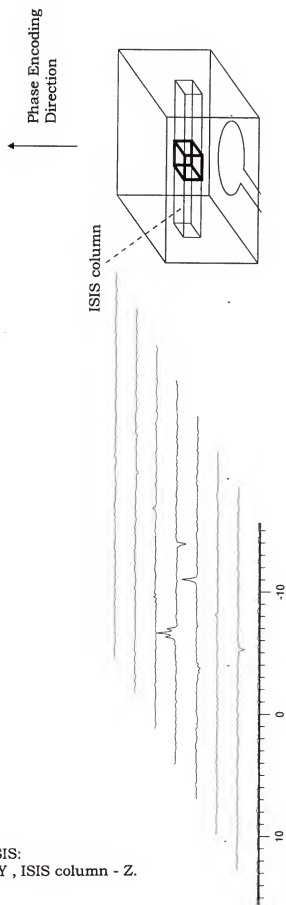


Figure 5.7(b) ^{31}P spectra by 1D CSI/2D ISIS:
 Phase encoding direction - Y , ISIS column - Z.

FILE : P03584.1-2-3-4
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 DATE : Mar 1 14:27:45 1997
 CF : 63.90 MHz
 SW : 2000.0
 SIZE : 2048 x 8
 PNTS : 1 to 2048
 LINES : 1 to 8
 CHAN : 1

97

Phase Encoding
 Direction

ISIS column

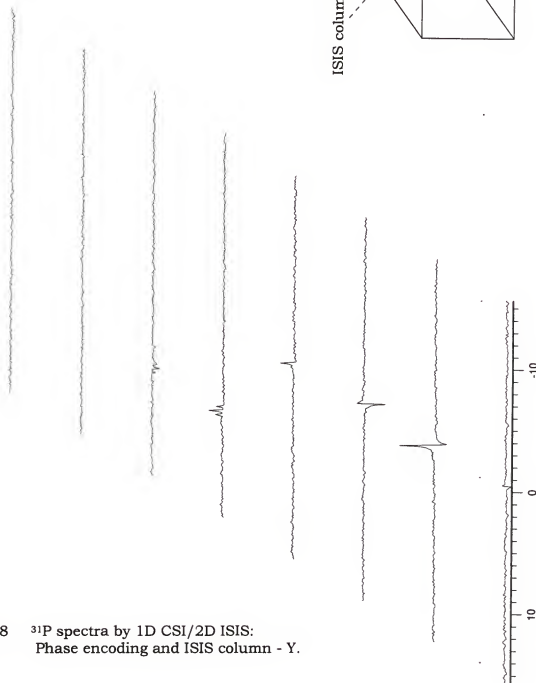
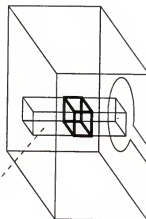


Figure 5.8 ^{31}P spectra by 1D CSI/2D ISIS:
 Phase encoding and ISIS column - Y.

FILE : P11776.I.6-7-8
 -9-10-11-12-13
 DATE : Mar 1 13:30:08 1997
 CF : 63.90 MHz
 SW : 2000.0
 SIZE : 2048 x 8
 PNTS : 1 to 2048
 LINES : 1 to 8
 CHAN : 1

98

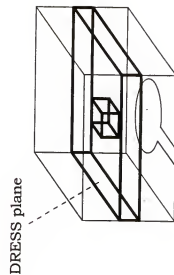
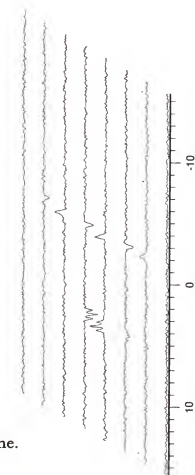


Figure 5.9 ^{31}P spectra by 1D CSI/DRESS:
 Phase encoding - Y, slice selection -XZ plane.

FILE : P071681-37

DATE : May 6 17:53:02 1997

CF : 63.90 MHz

SW : 2000.0

SIZE : 4096

PNTS : 1 to 4096

LINES : 1 to 1

CHAN : 1

MDPA

H₃PO₄

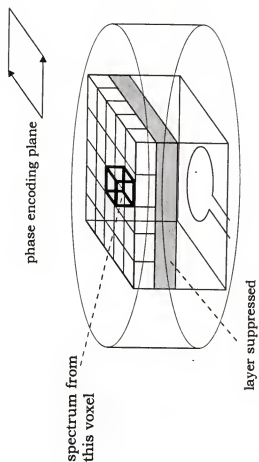
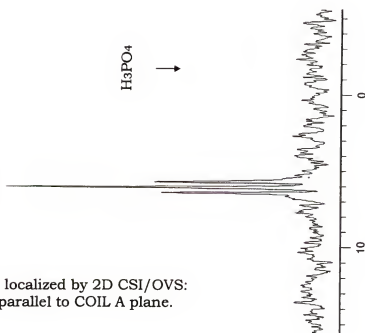


Figure 5.10(a)

³¹P spectrum localized by 2D CSI/OVS:
CSI plane is parallel to COIL A plane.

FILE : P07168.I-35-36
 -37-38-39
 DATE : Jun 9 00:18:46 1997
 CF : 63.90 MHz
 SW : 2000.0
 SIZE : 2048 x 5
 PNTS : 1 to 2048
 LINES : 1 to 5
 CHAN : 1

100

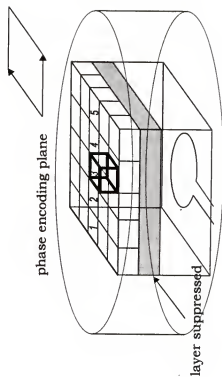
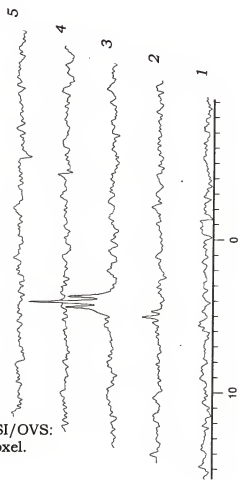


Figure 5.10(b)

^{31}P spectra along X from 2D CSI/OVS:
 MDPA bottle is in the center voxel.

FILE : P07168.I-21-29
 -37-45-53
 DATE : Jun 9 00:20:57 1997
 CF : 63.90 MHz
 SW : 2000.0
 SIZE : 2048 x 5
 PNTS : 1 to 2048
 LINES : 1 to 5
 CHAN : 1

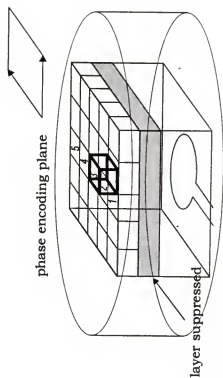
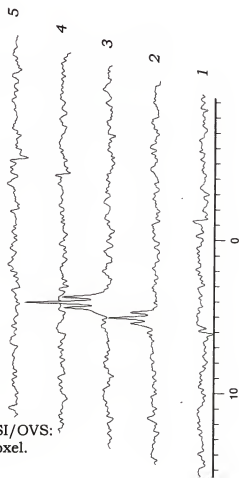


Figure 5.10(c)

^{31}P spectra along Z from 2D CSI/OVS:
 MDPa bottle is in the center voxel.

FILE : P07168.I-35-36
 -38-39-53-45-2
 DATE : May 6 19:22:37 1997
 CF : 63.90 MHz
 SW : 2000.0
 SIZE : 4096 x 12
 PNTS : 1 to 4096
 LINES : 1 to 12
 CHAN : 1

102

12

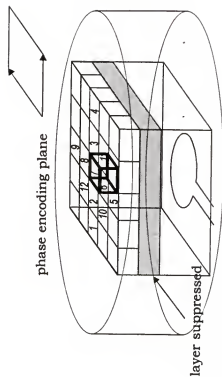
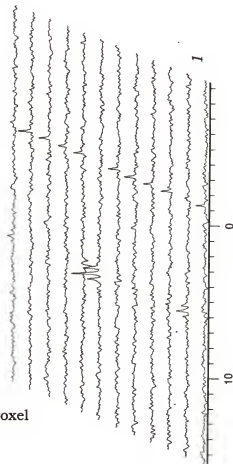


Figure 5.10(d) ^{31}P spectra from the center MDPA voxel and surrounding voxels.

FILE : P05632.I-53-45
 -37-29-21
 DATE : Jun 9 00:55:00 1997
 CF : 63.90 MHz
 SW : 2000.0
 SIZE : 1024 x 5
 PNTS : 1 to 1024
 LINES : 1 to 5
 CHAN : 1

103

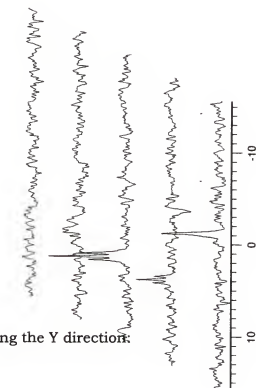
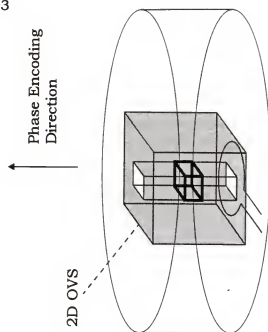


Figure 5.11

1D CSI/2D OVS ^{31}P spectra along the Y direction;
 2D OVS in the X-Z- direction.

FILE : G01464.001.000
 000000333
 DATE : Jun 8 01:28:22 1997
 CF : 25.87 MHz
 SW : 2000.0
 SIZE : 2048
 PNTS : 1 to 2048
 LINES : 1 to 1
 CHAN : 1

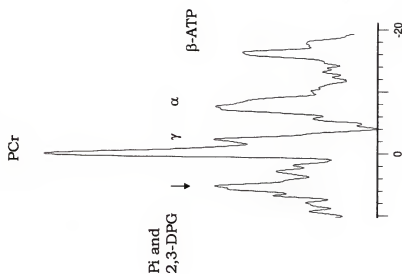


Figure 5.12(a)

^{31}P spectra from the left ventricular myocardium:
 2D OVS/1D ISIS technique with a single O/S pulse was used.

FILE : G01465.001.000
 000000333
 DATE : Jun 8 01:38:12 1997
 CF : 25.87 MHz
 SW : 2000.0
 SIZE : 2048
 PNTS : 1 to 2048
 LINES : 1 to 1
 CHAN : 1

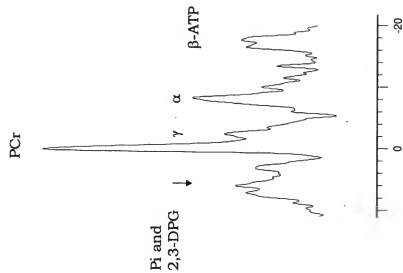


Figure 5.12(b)

^{31}P spectra from the left ventricular myocardium:
 2D OVS/1D ISIS technique with three OVS pulses was used.

FILE : G01468.001.000
 000000333
 DATE : Jun 8 01:58:40 1997
 CF : 25.87 MHz
 SW : 2000.0
 SIZE : 2048
 PNTS : 1 to 2048
 LINES : 1 to 1
 CHAN : 1

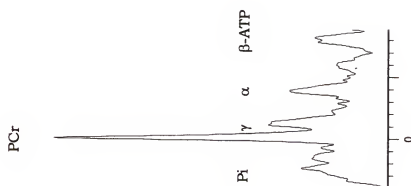


Figure 5.12(c)

^{31}P spectra from the chest muscle:
 2D OVS/1D ISIS technique with three OVS pulses was used.

FILE : P05632.I-5

DATE : May 14 15:29:14 1997

CF : 25.89 MHz

SW : 2000.0

SIZE : 2048

PNTS : 1 to 2048

LINES : 1 to 1

CHAN : 1

107

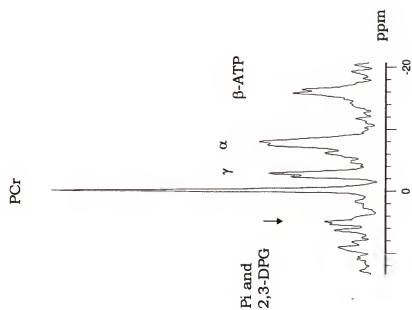


Figure 5.13(a)

^{31}P spectrum from the left ventricular myocardium
1D CSI/OVS technique was used.

FILE : P05632.1-1-2-3
 -4-5-6-7
 DATE : Jun 9 00:42:05 1997
 CF : 63.90 MHz
 SW : 2000.0
 SIZE : 1024 x 7
 PNTS : 229 to 857
 LINES : 1 to 7
 CHAN : 1

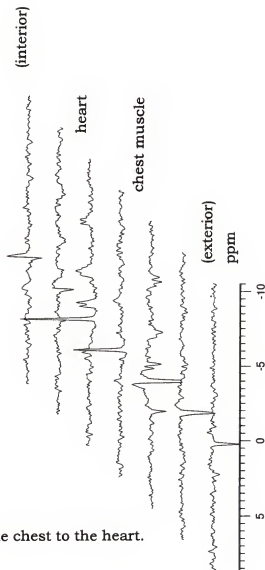


Figure 5.13(b)

^{31}P 1D CSI spectra from the chest to the heart.

FILE : P05632.I-3

DATE : May 14 15:28:30 1997

CF : 25.89 MHz

SW : 2000.0

SIZE : 2048

PNTS : 21 to 2048

LINES : 1 to 1

CHAN : 1

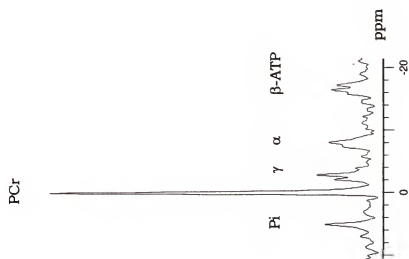


Figure 5.13(c)

^{31}P spectrum from the chest skeletal muscle:
1D CSI/OVS technique was used.

FILE : P05632.I-1-2-3
 -4-5-6-7
 DATE : Jun 9 00:45:11 1997
 CF : 63.90 MHz
 SW : 2000.0
 SIZE : 1024 x 7
 PNTS : 229 to 857
 LINES : 1 to 7
 CHAN : 1

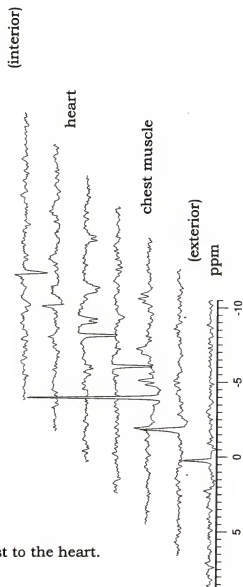


Figure 5.13(d) ^{31}P 1D CSI spectra from the chest to the heart.

CHAPTER 6 SUMMARY AND CONCLUSION

In an attempt to provide ^{31}P cardiac MR spectroscopy for the study of myocardial high-energy phosphate metabolism using a 1.5 tesla whole body imager, it was shown that the ^{31}P MR signal localized to the anterior myocardium can be acquired by combining the proper MR probe and pulse sequences designed for cardiac spectroscopy.

MR Probe

The surface coil was selected as the main MR probe for detecting ^{31}P MR signals due to its sensitivity to the signal from the intact human heart. The diameter of the surface coil for reception was 7.5 cm for the purpose of maximizing the signal-to-noise ratio at the usual depth of the anterior myocardial region and assuming that the subject is the dominant noise source.

Two surface coils were built : COIL A was used as both transmitter and receiver because of the convenience in designing and mounting and of phase coherence between transmitter and receiver. For B_0 field manual shimming, COIL A was tuned to the proton resonance frequency. A doubly tuned circuit based on Schnall's design was built and used. COIL B was designed for the purpose of producing a more homogeneous B_1 transmission field. This coil set consisted of two coils - one for reception, the other one for transmission coaxially positioned to the receiver coil. Mutual interference between the two coils was blocked by crossed diode and choke inductance circuitry.

These two coils obtained similar signal-to-noise ratio. COIL A could be more easily mounted on the chest in the supine position and had better filling characteristics. COIL B provided uniform B_1 field and was less sensitive to transmitter gain variation, which was advantageous when the scan parameters were adjusted for each human subject.

Localization Technique

Improvement in spatial selectivity was achieved by presaturation of the signal from outside the region-of-interest. Saturation pulses were designed for the suppression of the MR signals in the outer volume. The cosine-sinc amplitude modulation pulse was generated as a first saturation pulse. Using more than one consecutive pulse enhanced the level of presaturation. Excitation for saturation was followed by a gradient for dephasing. A single dephasing gradient cannot perfectly dephase the pre-excited coherence in a given pulse width of 2 ms. However, using paired dephasing gradients, instead of a single directional gradient, improved dephasing.

Another saturation pulse was generated based upon the Shinnar-Le Roux (SLR) algorithm. Because it is advantageous for the saturation pulse to produce the magnetization dephased as much as possible, the saturation pulse was generated using the maximum-phase pulse option.

Outer volume suppression using a cosine-sinc pulse did not work properly along the coil axis because of the large variation of the B_1 field. In this direction, it is advantageous to use one dimensional ISIS localization with a B_1 -insensitive hyperbolic secant adiabatic pulse. A hybrid of 2D OVS and 1D ISIS was developed. OVS was applied to the slices for outside the ROI vertical to the

coil plane in the X and Z directions and the ISIS pulse for a column standing perpendicular to the coil plane (along the vertical or Y axis). Alternation of the polarity of the dephasing gradient improves signal-to-noise ratio and phasing.

Spectroscopic imaging with various localization schemes, such as 3D-ISIS/1D-CSI, 2D-CSI, 2D-ISIS/1D-CSI, 1D or 2D CSI with spatial saturation were tested. Among these combinations, 2D-ISIS/1D-CSI was an effective combination for the phantom study but did not work properly for heart because of cardiac motion. Instead, CSI combined with spatial saturation was most suitable for cardiac spectroscopy.

Phosphorus-31 Cardiac MR in Vivo Spectroscopy

Cardiac ECG gating enables the control of acquisition so that it occurs only during the same phase of the cardiac cycle. Cardiac gating minimizes the motion artifact from the contractile motion of the heart although it can not eliminate all motion artifacts. With triggering accomplished by detecting the R wave, a scout image and image guided localized spectroscopy was successfully obtained. The quality of the spectrum was improved when the triggering was positioned in the middle of the systole-diastole period.

Both manual shimming using the STEAM technique and AUTOSHIM were used to homogenize the B_0 field in the frontal left ventricular myocardium. When the STEAM sequence was used, COIL A doubly tuned to ^1H and ^{31}P MR frequencies was used instead of the body coil.

Phosphorus-31 spectra were obtained from the anterior myocardium using either 2D-OVS/1D-ISIS hybrid pulse, or CSI/OVS. These pulses localized the MR signals from the tissues at various depths. About 20 to 25 minutes

acquisition can provide reasonable spectral data for either sequences. By using the outer volume presaturation technique, ^{31}P spectra from the heart were obtained effectively. **This is the first time the OVS technique has been applied to cardiac studies.** The 2D-OVS/1D-ISIS hybrid sequence shows better signal-to-noise ratio than the 3D ISIS sequence in which the motion severely compromised the localization such that no useful cardiac spectra could be obtained. The 2D-OVS/1D-ISIS hybrid can be used most effectively when the heart is situated not too deep in the chest where the cos-sinc pulse can deliver sufficient power to saturate. **Chemical shift imaging combined with outer volume presaturation is the only available technique for the deep seated heart. Spatially resolved spectroscopic information was obtained from the phase encoded signals acquired from the entire volume simultaneously.**

The PCr/ATP ratio was evaluated after spectral analysis. The partial saturation effect was taken into account. It was possible to measure directly partial saturation effects for each human volunteer using non-selective acquisition. The PCr/ATP ratio was comparable to studies done by other investigators. Blood contamination affects the localized spectrum in the Pi, PME and ATP peak region. Future work will have to be directed toward eliminating the blood contamination including proton decoupled ^{31}P spectroscopy which enables the inorganic phosphate peak to be differentiated from the 2,3-DPG peaks to evaluate the amount of ATP contamination by blood.

APPENDIX A
Matlab® M-file for Saturation Pulse Design

```
%      by Hee-Won Kim, University of Florida, 10-18-96
%
%      The modulation frequency NUCOS of  $\cos(2\pi \cdot \text{NUCOS} \cdot t)$ 
%      determines the width ROI(inner region), such that
%      the diameter of the ROI increases as nucos increases.
%
%      The frequency NUSINC, the width of the central lobe of the sinc
%      function determines the diameter of the outer region to be excited.
%
%      NUMBER : pulse resolution
%      NUSINC : modulation frequency of sinc
%      NUCOS  : modulation frequency of cos
%      BFILE  : output binary file
%      TFILE  : output text file
%      RAD =  $2\pi$  over NUMBER

function y=cossincepic(Number,Nucos,Nusinc,Bfile,Tfile);

% ----- radian set -----
NUM=(Number-1)/2;
N=[-NUM:NUM];
RAD=2*pi*N/Number;

%----- sinc*cos -----
ts=RAD*Nusinc;tc=RAD*Nucos;
S=sinc(ts);Q=cos(tc);
WAVE=S.*Q;
```

```

subplot(311),plot(RAD,WAVE);

%----- Fourier Transform -----
F=fft(WAVE);F(1)=[];L=length(F);
power=abs(F(1:L/2)).^2;nyquist=1/2;freq=(1:L/2)/(L/2)*nyquist;
subplot(312),plot(freq,power);
subplot(313),plot(freq(1:30),power(1:30));

%----- binary and text file for EPIC -----
%----- binary -----
B=fopen(Bfile,'wb');
IWAVE=WAVE*32767;
count=fwrite(B,IWAVE,'short')

%----- text -----
BO=fopen(Bfile);
[READ,count]=fread(BO,[inf],'short');
T=fopen(Tfile,'wt');
count=fprintf(T,'%10i',READ)
%
%
function y=cossinc(Number,Nucos,Nusinc);

% ----- radian set -----
NUM=(Number-1)/2;
N=[-NUM:NUM];
RAD=2*pi*N/Number;

%----- sinc*cos -----
ts=RAD*Nusinc;tc=RAD*Nucos;
S=sinc(ts);Q=cos(tc);
WAVE=S.*Q;
subplot(311),plot(RAD,WAVE);

```

```

%----- Fourier Transform -----
F=fft(WAVE);F(1)=[];L=length(F);
power=abs(F(1:L/2)).^2;nyquist=1/2;freq=(1:L/2)/(L/2)*nyquist;
subplot(312),plot(freq,power);
subplot(313),plot(freq(1:30),power(1:30));

%      by Hee-Won Kim, University of Florida, 10-22-96
%
%      To read GE EPIC pulse format and to convert it to 'vnmr' format
%
%      BINFILE : file to be converted
%      FACTOR   : multiplication factor
%      PHASE flag : 0(amplitude), 1(phase)

%      tfile    : text file generated (EPIC)
%      btemp     : temporary binary file
%      tfileamp  : amplitude text file (vnmr)
%      tfilephase : phase text file (vnmr)
%

function y=readepicpulse(BinFile,Factor,PhaseFlag);

% ----- open binary file / transpose -----

BO=fopen(BinFile);
[READHDR,count]=fread(BO,['f','short']);
READHDR = READHDR*Factor;

count

% ----- file with HEADER -----
% Header file has 32 values in front and 3 values at the end

```

```

% Elements shifted up by 32 elements
%

N=count-35

for i = 1:N,
    READ(i) = READHDR(i+32);
    READ(i) = round(READ(i));
end

MESH=[-N/2+0.5:N/2-0.5];
plot(MESH,READ)

% ----- EPIC text file -----
T=fopen('tfile','wt');count=fprintf(T,'%10i',READ)

%----- 'pulsetool' format -----
NM1=[-N/2-0.5:N/2-1.5];
ONE=MESH-NM1;

if PhaseFlag == 0
    ONEZERO=[0 0 1]*ONE;
    WAVEREAD=[0 1 0]*READ;
elseif PhaseFlag == 1
    ONEZERO=[0 0 1]*ONE;
    WAVEREAD=[1 0 0]*READ;
end

WAVEPULSE=WAVEREAD+ONEZERO;

%----- generating text files for vnmr format -----
B=fopen('btemp','wb');count=fwrite(B,WAVEPULSE,'short');
BO=fopen('btemp');

```

```
[READOUT,count]=fread(BO,[inf],'short');
```

```
if PhaseFlag == 0
```

```
    T=fopen('tfileamp','wt');
```

```
elseif PhaseFlag == 1
```

```
    T=fopen('tfilephase','wt');
```

```
end
```

```
count=fprintf(T,'%10i %10i %10i\n',READOUT);
```

APPENDIX B
Cos-Sinc Saturation Pulse

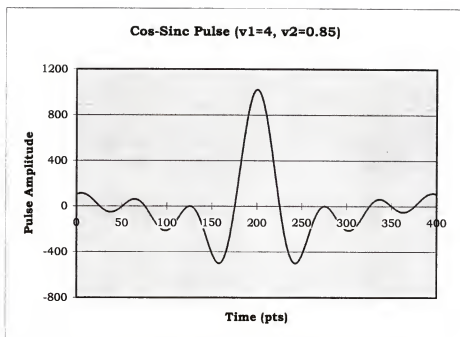
<u>Phase</u>	<u>Amplitude</u>	<u>Phase</u>	<u>Amplitude</u>	<u>Phase</u>	<u>Amplitude</u>
0	106	0	-48	0	58
0	108	0	-50	0	55
0	110	0	-52	0	51
0	112	0	-53	0	45
0	112	0	-53	0	39
0	112	0	-53	0	32
0	111	0	-52	0	24
0	110	0	-50	0	15
0	107	0	-47	0	5
0	104	0	-43	0	-5
0	101	0	-39	0	-16
0	96	0	-34	0	-28
0	91	0	-29	0	-40
0	86	0	-24	0	-53
0	80	0	-17	0	-66
0	73	0	-11	0	-79
0	66	0	-4	0	-92
0	59	0	2	0	-104
0	51	0	8	0	-117
0	43	0	15	0	-130
0	35	0	22	0	-141
0	27	0	28	0	-153
0	19	0	34	0	-163
0	11	0	40	0	-173
0	3	0	45	0	-182
0	-3	0	50	0	-190
0	-11	0	54	0	-197
0	-18	0	57	0	-203
0	-24	0	60	0	-208
0	-30	0	61	0	-212
0	-35	0	62	0	-214
0	-40	0	62	0	-215
0	-44	0	60	0	-214

Phase	Amplitude	Phase	Amplitude	Phase	Amplitude
0	-213	0	-347	0	927
0	-210	0	-370	0	954
0	-206	0	-391	0	976
0	-200	0	-412	0	994
0	-194	0	-430	0	1008
0	-186	0	-447	0	1017
0	-177	0	-462	0	1022
0	-168	0	-475	0	1022
0	-158	0	-485	0	1017
0	-147	0	-493	0	1008
0	-135	0	-498	0	994
0	-123	0	-499	0	976
0	-111	0	-498	0	954
0	-99	0	-493	0	927
0	-87	0	-486	0	896
0	-75	0	-474	0	862
0	-63	0	-459	0	823
0	-52	0	-441	0	782
0	-42	0	-419	0	737
0	-32	0	-394	0	690
0	-23	0	-365	0	640
0	-16	0	-333	0	589
0	-10	0	-297	0	535
0	-5	0	-259	0	480
0	-2	0	-217	0	423
0	0	0	-173	0	366
0	0	0	-126	0	309
0	-1	0	-77	0	251
0	-5	0	-26	0	194
0	-10	0	26	0	137
0	-17	0	81	0	81
0	-26	0	137	0	26
0	-37	0	194	0	-26
0	-50	0	251	0	-77
0	-64	0	309	0	-126
0	-80	0	366	0	-173
0	-97	0	423	0	-217
0	-116	0	480	0	-259
0	-137	0	535	0	-297
0	-158	0	589	0	-333
0	-180	0	640	0	-365
0	-204	0	690	0	-394
0	-227	0	737	0	-419
0	-251	0	782	0	-441
0	-276	0	823	0	-459
0	-300	0	862	0	-474
0	-324	0	896	0	-486

Phase	Amplitude	Phase	Amplitude	Phase	Amplitude
0	-493	0	-99	0	60
0	-498	0	-111	0	62
0	-499	0	-123	0	62
0	-498	0	-135	0	61
0	-493	0	-147	0	60
0	-485	0	-158	0	57
0	-475	0	-168	0	54
0	-462	0	-177	0	50
0	-447	0	-186	0	45
0	-430	0	-194	0	40
0	-412	0	-200	0	34
0	-391	0	-206	0	28
0	-370	0	-210	0	22
0	-347	0	-213	0	15
0	-324	0	-214	0	8
0	-300	0	-215	0	2
0	-276	0	-214	0	-4
0	-251	0	-212	0	-11
0	-227	0	-208	0	-17
0	-204	0	-203	0	-24
0	-180	0	-197	0	-29
0	-158	0	-190	0	-34
0	-137	0	-182	0	-39
0	-116	0	-173	0	-43
0	-97	0	-163	0	-47
0	-80	0	-153	0	-50
0	-64	0	-141	0	-52
0	-50	0	-130	0	-53
0	-37	0	-117	0	-53
0	-26	0	-104	0	-53
0	-17	0	-92	0	-52
0	-10	0	-79	0	-50
0	-5	0	-66	0	-48
0	-1	0	-53	0	-44
0	0	0	-40	0	-40
0	0	0	-28	0	-35
0	-2	0	-16	0	-30
0	-5	0	-5	0	-24
0	-10	0	5	0	-18
0	-16	0	15	0	-11
0	-23	0	24	0	-3
0	-32	0	32	0	3
0	-42	0	39	0	11
0	-52	0	45	0	19
0	-63	0	51	0	27
0	-75	0	55	0	35
0	-87	0	58	0	43

Phase	Amplitude
-------	-----------

0	51
0	59
0	66
0	73
0	80
0	86
0	91
0	96
0	101
0	104
0	107
0	110
0	111
0	112
0	112
0	112
0	110
0	108
0	106



APPENDIX C
SLR Maximum Phase Saturation Pulse

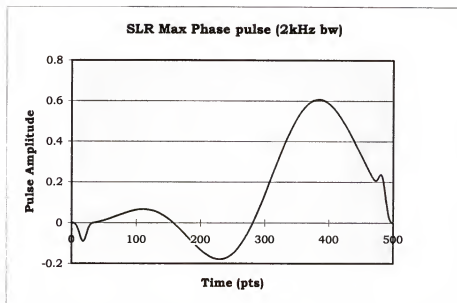
Amplitude			
0.0000	0.0004	0.0308	0.0634
0.0000	0.0010	0.0320	0.0640
-0.0004	0.0015	0.0332	0.0645
-0.0014	0.0021	0.0344	0.0650
-0.0031	0.0027	0.0355	0.0654
-0.0058	0.0033	0.0367	0.0657
-0.0096	0.0040	0.0379	0.0660
-0.0148	0.0047	0.0390	0.0663
-0.0217	0.0054	0.0401	0.0664
-0.0302	0.0061	0.0412	0.0666
-0.0400	0.0066	0.0424	0.0666
-0.0504	0.0074	0.0435	0.0666
-0.0609	0.0083	0.0446	0.0665
-0.0708	0.0092	0.0457	0.0664
-0.0793	0.0101	0.0468	0.0662
-0.0860	0.0110	0.0478	0.0659
-0.0902	0.0119	0.0489	0.0656
-0.0912	0.0130	0.0499	0.0652
-0.0888	0.0139	0.0509	0.0648
-0.0836	0.0150	0.0519	0.0643
-0.0762	0.0160	0.0529	0.0638
-0.0671	0.0171	0.0539	0.0633
-0.0571	0.0182	0.0548	0.0627
-0.0468	0.0192	0.0558	0.0621
-0.0367	0.0204	0.0567	0.0614
-0.0275	0.0215	0.0576	0.0607
-0.0198	0.0226	0.0584	0.0600
-0.0137	0.0238	0.0592	0.0591
-0.0090	0.0249	0.0600	0.0582
-0.0055	0.0261	0.0608	0.0572
-0.0031	0.0273	0.0615	0.0562
-0.0014	0.0285	0.0622	0.0550
-0.0003	0.0296	0.0628	0.0538

Amplitude

0.0525	-0.0694	-0.1780	-0.0465
0.0511	-0.0727	-0.1783	-0.0406
0.0496	-0.0760	-0.1785	-0.0345
0.0481	-0.0794	-0.1785	-0.0283
0.0465	-0.0827	-0.1784	-0.0220
0.0448	-0.0860	-0.1782	-0.0155
0.0430	-0.0893	-0.1778	-0.0090
0.0413	-0.0925	-0.1773	-0.0024
0.0394	-0.0957	-0.1767	0.0043
0.0375	-0.0990	-0.1760	0.0111
0.0355	-0.1022	-0.1751	0.0180
0.0335	-0.1053	-0.1742	0.0250
0.0315	-0.1085	-0.1730	0.0322
0.0293	-0.1116	-0.1718	0.0394
0.0272	-0.1147	-0.1704	0.0467
0.0249	-0.1177	-0.1688	0.0537
0.0226	-0.1207	-0.1672	0.0612
0.0203	-0.1236	-0.1654	0.0687
0.0179	-0.1265	-0.1634	0.0763
0.0154	-0.1294	-0.1613	0.0839
0.0129	-0.1321	-0.1591	0.0917
0.0104	-0.1349	-0.1568	0.0994
0.0078	-0.1376	-0.1543	0.1073
0.0051	-0.1402	-0.1516	0.1151
0.0024	-0.1427	-0.1488	0.1231
-0.0004	-0.1451	-0.1458	0.1310
-0.0032	-0.1476	-0.1427	0.1390
-0.0061	-0.1499	-0.1395	0.1471
-0.0090	-0.1522	-0.1361	0.1552
-0.0120	-0.1544	-0.1326	0.1633
-0.0149	-0.1565	-0.1289	0.1715
-0.0179	-0.1586	-0.1251	0.1797
-0.0207	-0.1605	-0.1212	0.1880
-0.0238	-0.1624	-0.1171	0.1962
-0.0269	-0.1642	-0.1130	0.2044
-0.0300	-0.1659	-0.1086	0.2127
-0.0332	-0.1675	-0.1042	0.2210
-0.0364	-0.1690	-0.0996	0.2292
-0.0396	-0.1704	-0.0949	0.2375
-0.0428	-0.1717	-0.0900	0.2457
-0.0461	-0.1729	-0.0850	0.2540
-0.0494	-0.1740	-0.0799	0.2622
-0.0527	-0.1749	-0.0746	0.2704
-0.0560	-0.1758	-0.0693	0.2786
-0.0594	-0.1765	-0.0638	0.2867
-0.0627	-0.1771	-0.0581	0.2949
-0.0660	-0.1776	-0.0524	0.3030

Amplitude

0.3111	0.5864	0.5343	0.2584
0.3191	0.5889	0.5298	0.2522
0.3271	0.5914	0.5252	0.2461
0.3351	0.5936	0.5206	0.2400
0.3430	0.5957	0.5158	0.2340
0.3508	0.5975	0.5108	0.2281
0.3586	0.5992	0.5059	0.2224
0.3663	0.6008	0.5008	0.2172
0.3740	0.6022	0.4956	0.2128
0.3815	0.6034	0.4904	0.2095
0.3890	0.6044	0.4851	0.2073
0.3964	0.6053	0.4797	0.2067
0.4037	0.6061	0.4742	0.2078
0.4109	0.6067	0.4687	0.2108
0.4181	0.6071	0.4631	0.2156
0.4252	0.6074	0.4574	0.2215
0.4322	0.6075	0.4516	0.2273
0.4390	0.6075	0.4458	0.2324
0.4458	0.6073	0.4399	0.2357
0.4525	0.6069	0.4339	0.2366
0.4590	0.6064	0.4279	0.2341
0.4655	0.6057	0.4219	0.2272
0.4719	0.6048	0.4158	0.2154
0.4781	0.6038	0.4096	0.1990
0.4842	0.6026	0.4034	0.1791
0.4902	0.6013	0.3972	0.1567
0.4960	0.5997	0.3910	0.1330
0.5017	0.5981	0.3847	0.1091
0.5073	0.5962	0.3784	0.0859
0.5128	0.5942	0.3721	0.0647
0.5181	0.5920	0.3658	0.0464
0.5233	0.5897	0.3594	0.0318
0.5283	0.5872	0.3531	0.0207
0.5332	0.5846	0.3467	0.0125
0.5380	0.5819	0.3404	0.0067
0.5426	0.5790	0.3339	0.0031
0.5471	0.5759	0.3276	0.0010
0.5515	0.5727	0.3212	0.0001
0.5557	0.5694	0.3148	0.0000
0.5597	0.5660	0.3085	
0.5636	0.5625	0.3021	
0.5673	0.5588	0.2958	
0.5709	0.5550	0.2895	
0.5743	0.5511	0.2832	
0.5776	0.5471	0.2770	
0.5807	0.5429	0.2707	
0.5836	0.5387	0.2645	



APPENDIX D
Phase Modulated BIR-4 Pulse

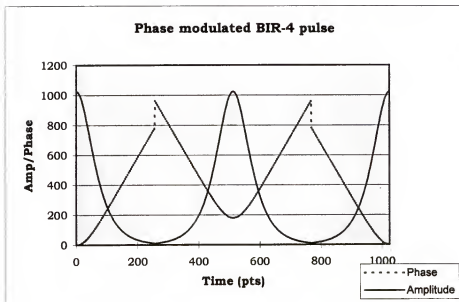
The first half of the symmetric pulse is listed.

Phase	Amplitude	Phase	Amplitude	Phase	Amplitude
0.0	1023	38.1	822	127.0	488
0.1	1023	40.2	812	130.1	479
0.2	1022	42.4	802	133.2	470
0.4	1021	44.6	791	136.3	462
0.7	1019	46.9	781	139.5	453
1.1	1018	49.2	770	142.7	445
1.5	1015	51.6	760	145.9	436
2.0	1012	54.0	749	149.1	428
2.6	1009	56.4	738	152.3	420
3.3	1005	58.9	728	155.5	412
4.0	1001	61.4	717	158.7	405
4.8	997	63.9	707	162.0	397
5.6	992	66.5	696	165.2	389
6.6	987	69.1	685	168.5	382
7.6	981	71.8	675	171.7	375
8.6	975	74.5	664	175.0	367
9.8	969	77.2	654	178.3	360
10.9	962	79.9	643	181.6	353
12.2	955	82.7	633	184.9	347
13.5	948	85.5	623	188.3	340
14.9	941	88.3	613	191.6	333
16.4	933	91.1	602	194.9	327
17.9	925	94.0	592	198.3	320
19.4	916	96.9	582	201.6	314
21.0	908	99.8	572	205.0	308
22.7	899	102.7	563	208.3	302
24.5	890	105.7	553	211.7	296
26.3	881	108.7	543	215.1	290
28.1	871	111.7	534	218.5	284
30.0	862	114.7	524	221.8	279
31.9	852	117.7	515	225.2	273
33.9	842	120.8	506	228.6	268
36.0	832	123.9	497	232.0	263

Phase	Amplitude	Phase	Amplitude	Phase	Amplitude
235.4	257	398.5	98	563.6	37
238.8	252	402.0	96	567.1	36
242.3	247	405.5	94	570.6	36
245.7	242	409.0	92	574.1	35
249.1	237	412.5	90	577.7	34
252.5	233	416.0	89	581.2	33
256.0	228	419.6	87	584.7	33
259.4	223	423.1	85	588.2	32
262.8	219	426.6	83	591.7	31
266.3	215	430.1	82	595.2	31
269.7	210	433.6	80	598.8	30
273.2	206	437.1	78	602.3	30
276.6	202	440.6	77	605.8	29
280.1	198	444.1	75	609.3	28
283.5	194	447.6	74	612.8	28
287.0	190	451.1	72	616.4	27
290.4	186	454.6	71	619.9	27
293.9	182	458.2	69	623.4	26
297.4	179	461.7	68	626.9	26
300.8	175	465.2	66	630.4	25
304.3	171	468.7	65	633.9	24
307.8	168	472.2	64	637.5	24
311.2	165	475.7	62	641.0	23
314.7	161	479.2	61	644.5	23
318.2	158	482.7	60	648.0	23
321.7	155	486.3	59	651.5	22
325.2	152	489.8	57	655.0	22
328.6	148	493.3	56	658.6	21
332.1	145	496.8	55	662.1	21
335.6	142	500.3	54	665.6	20
339.1	140	503.8	53	669.1	20
342.6	137	507.3	52	672.6	19
346.1	134	510.9	51	676.2	19
349.6	131	514.4	50	679.7	19
353.1	129	517.9	49	683.2	18
356.5	126	521.4	48	686.7	18
360.0	123	524.9	47	690.2	18
363.5	121	528.4	46	693.8	17
367.0	118	531.9	45	697.3	17
370.5	116	535.5	44	700.8	16
374.0	114	539.0	43	704.3	16
377.5	111	542.5	42	707.8	16
381.0	109	546.0	41	711.3	16
384.5	107	549.5	40	714.9	15
388.0	105	553.0	39	718.4	15
391.5	102	556.6	39	721.9	15
395.0	100	560.1	38	725.4	14

Phase	Amplitude	Phase	Amplitude	Phase	Amplitude
728.9	14	852.6	19	687.3	52
732.5	14	849.1	20	683.8	53
736.0	13	845.6	20	680.3	54
739.5	13	842.1	21	676.8	55
743.0	13	838.6	21	673.3	56
746.5	13	835.0	22	669.8	57
750.1	12	831.5	22	666.3	59
753.6	12	828.0	23	662.7	60
757.1	12	824.5	23	659.2	61
760.6	12	821.0	23	655.7	62
764.1	11	817.5	24	652.2	64
767.6	11	813.9	24	648.7	65
771.2	11	810.4	25	645.2	66
774.7	11	806.9	26	641.7	68
778.2	10	803.4	26	638.2	69
781.7	10	799.9	27	634.6	71
961.7	10	796.4	27	631.1	72
958.2	10	792.8	28	627.6	74
954.7	11	789.3	28	624.1	75
951.2	11	785.8	29	620.6	77
947.6	11	782.3	30	617.1	78
944.1	11	778.8	30	613.6	80
940.6	12	775.2	31	610.1	82
937.1	12	771.7	31	606.6	83
933.6	12	768.2	32	603.1	85
930.1	12	764.7	33	599.6	87
926.5	13	761.2	33	596.0	89
923.0	13	757.7	34	592.5	90
919.5	13	754.1	35	589.0	92
916.0	13	750.6	36	585.5	94
912.5	14	747.1	36	582.0	96
908.9	14	743.6	37	578.5	98
905.4	14	740.1	38	575.0	100
901.9	15	736.6	39	571.5	102
898.4	15	733.0	39	568.0	105
894.9	15	729.5	40	564.5	107
891.3	16	726.0	41	561.0	109
887.8	16	722.5	42	557.5	111
884.3	16	719.0	43	554.0	114
880.8	16	715.5	44	550.5	116
877.3	17	711.9	45	547.0	118
873.8	17	708.4	46	543.5	121
870.2	18	704.9	47	540.0	123
866.7	18	701.4	48	536.5	126
863.2	18	697.9	49	533.1	129
859.7	19	694.4	50	529.6	131
856.2	19	690.9	51	526.1	134

Phase	Amplitude	Phase	Amplitude	Phase	Amplitude
522.6	137	361.6	353	224.6	791
519.1	140	358.3	360	222.4	802
515.6	142	355.0	367	220.2	812
512.1	145	351.7	375	218.1	822
508.6	148	348.5	382	216.0	832
505.2	152	345.2	389	213.9	842
501.7	155	342.0	397	211.9	852
498.2	158	338.7	405	210.0	862
494.7	161	335.5	412	208.1	871
491.2	165	332.3	420	206.3	881
487.8	168	329.1	428	204.5	890
484.3	171	325.9	436	202.7	899
480.8	175	322.7	445	201.0	908
477.4	179	319.5	453	199.4	916
473.9	182	316.3	462	197.9	925
470.4	186	313.2	470	196.4	933
467.0	190	310.1	479	194.9	941
463.5	194	307.0	488	193.5	948
460.1	198	303.9	497	192.2	955
456.6	202	300.8	506	190.9	962
453.2	206	297.7	515	189.8	969
449.7	210	294.7	524	188.6	975
446.3	215	291.7	534	187.6	981
442.8	219	288.7	543	186.6	987
439.4	223	285.7	553	185.6	992
436.0	228	282.7	563	184.8	997
432.5	233	279.8	572	184.0	1001
429.1	237	276.9	582	183.3	1005
425.7	242	274.0	592	182.6	1009
422.3	247	271.1	602	182.0	1012
418.8	252	268.3	613	181.5	1015
415.4	257	265.5	623	181.1	1018
412.0	263	262.7	633	180.7	1019
408.6	268	259.9	643	180.4	1021
405.2	273	257.2	654	180.2	1022
401.8	279	254.5	664	180.1	1023
398.5	284	251.8	675	180.0	1023
395.1	290	249.1	685		
391.7	296	246.5	696		
388.3	302	243.9	707		
385.0	308	241.4	717		
381.6	314	238.9	728		
378.3	320	236.4	738		
374.9	327	234.0	749		
371.6	333	231.6	760		
368.3	340	229.2	770		
364.9	347	226.9	781		



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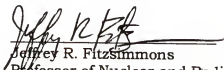
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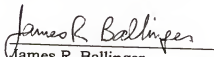
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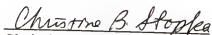
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